WHO/HAI Project on

Medicine Prices and Availability

Review Series on

Pharmaceutical Pricing Policies and Interventions

Working Paper 3:

The Regulation of Mark-ups in the Pharmaceutical Supply Chain

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May 2011

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WHO/HAI Project on Medicine Prices and Availability
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Abbreviations

ACT	Artemisinin combination therapy
CIF	Cost, Insurance and Freight
CMS	Central medical store
EML	Essential medicines list
EU	European Union
GST	General sales tax
HAI	Health Action International
HIC	High-income country
HMO	Health maintenance organisation
LIC	Low-income country
LMIC	Low- and middle-income country
L-MIC	Lower-middle-income country
MIC	Middle-income country
MSP	Manufacturer's selling price
ÖBIG	Gesundheit Österreich GmbH (Austrian Federal Institute for Healthcare)
OECD	Organisation for Economic Co-operation and Development
OTC	Over-the-counter
PPRI	Pharmaceutical Pricing and Reimbursement Information project of ÖBIG
SEP	Single Exit Price
UAE	United Arab Emirates
UK	United Kingdom
UMIC	Upper-middle-income country
USA	United States of America
VAT	Value-added tax
WHO	World Health Organization

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Foreword

WHO/HAI Project on Medicine Prices and Availability

Since 2001, the World Health Organization (WHO) and Health Action International (HAI) have been working in partnership to collect reliable evidence on medicine prices, availability, affordability and price components in low- and middle-income countries. To date over 80 medicine price and availability surveys have been completed or are underway using the WHO/HAI methodology, with results publicly available on the HAI website (www.haiweb.org/medicineprices). While this work continues to expand, the WHO/HAI project has evolved from supporting research to using the results to effect positive changes in related policies and interventions.

The results of the surveys confirm that substantial opportunities exist to increase availability, lower prices, and improve the affordability of medicines in all regions of the world and at all levels of economic development. However, it can be challenging to identify and prepare suitable lines of response.

At the request of national policy-makers, WHO/HAI and a group of international experts have developed guidance on various policies and interventions to increase medicine availability and make medicines more affordable, with a focus on low- and middle-income countries. This guidance takes the form of a series of in-depth reviews on pharmaceutical pricing policies (generics policies, external reference pricing, mark-up regulation, pharmacoeconomics and cost-plus pricing) and other related issues including the role of health insurance in the cost-effective use of medicines, encouraging competition, and sales taxes on medicines. The reviews are not meant to recommend one policy intervention over another, but rather provide guidance to policy-makers on the design and implementation of various policy approaches. For each review, a policy brief will be published that highlights key points from the review.

The results of the policy reviews show that relatively little has been published about the use of pharmaceutical pricing policies and interventions in low- and middle-income countries. Therefore, the review papers are published as working drafts, to be developed as more becomes known on the use of these interventions in low-and middle-income countries. We welcome information and comments that will strengthen these reviews (please forward them to Margaret Ewen, Health Action International email marg@haiweb.org).

WHO and HAI would like to thank the authors of the papers, the reviewers, and all the national contributors who provided information on the use of the interventions in their country. We are also grateful to the members of the Pricing Policy Working Group who have shaped this work.

We hope these papers will be a useful resource, and encourage national policy-makers to tackle the challenge of developing and implementing policies and strategies that ensure universal access to affordable medicines.

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Executive summary

This paper reviews the literature on the regulation of pharmaceutical distribution mark-ups in low- and middle-income countries (LMICs) with a view to describing and analysing the current knowledge. A search was conducted of published literature indexed in PubMed and EconLit as well as grey literature.

Evidence of the regulation of mark-ups in the distribution chain in LMICs is sparse, not systematically collected, and often of poor quality where it exists.WHO pharmaceutical indicator survey data shows that around 60% of low-income countries report regulating wholesale or retail mark-ups in either the public or private sector. In middle-income countries, regulation in the public sector is of a comparable level. Data from medicine pricing and availability surveys undertaken using the WHO/HAI methodology suggest that fixed percentage mark-ups are most common in LMICs, with regressive mark-ups only applied in some higher income economies e.g. India, Iran.

Mark-up regulation is generally not used as a means to promote generic dispensing, and in LMICs it tends to include all medicines within the defined public or private sector. There is no reliable information available about the impact of mark-up regulation alone on medicine prices in LMICs. Enforcement of regulations is also seldom covered in the literature apart from a small number of accounts of varying degrees of lax enforcement in some countries.

There is limited information about the effect of mark-up regulation on the viability of distribution operations at importer, wholesale or retail level. However, in unregulated pharmaceutical settings, retail mark-ups in the private sector vary depending on distance from major urban centres. A fixed percentage mark-up appears the most common form of remuneration of retailers in LMICs and dispensing fees are uncommon. Apart from isolated mention of discounts and rebates, there was no evidence as to whether regulation of such commercial practices would be effective in reducing medicine prices.

The above information contrasts with the situation in high-income countries (HICs) where mark-ups or margins are commonly regulated in countries that have a national health system or other reimbursement mechanism for prescribed pharmaceuticals. This is usually part of comprehensive medicine price regulation which, as a whole, has been shown to reduce pharmaceutical expenditure in the short term. Retailer mark-ups appear more likely to be subject to regulation than wholesaler mark-ups in HICs and a variety of methods are used from simple flat percentage mark-ups through regressive scales combined with fixed fees or more complex formulae. High-income countries often focus their regulation on prescription medicines or those which are reimbursed. It is assumed that high-income countries have rigorous enforcement mechanisms.

Based on the literature available, the following key points were identified:

- Regulation of mark-ups as part of a comprehensive price regulation strategy probably will lead to reduced medicine prices. However, regulation of mark-ups without regulation of either the manufacturer's selling price or the retail selling price is unlikely to lead to reduced medicine prices.

- Regulation of mark-ups will probably have an effect on the viability of some operators in the pharmaceutical supply chain and may adversely impact the viability of operations in more remote areas or other health services that are cross-subsidized through higher mark-ups.

- Regulation of distribution mark-ups can have unintended impacts or consequences. Incentives and disincentives need to be mapped and potential unexpected effects considered.

- A reliable mechanism for monitoring the prices and sales of medicines in the appropriate sector or market is essential to be able to judge the effects of pricing regulations, both intended and unintended.

- It is possible to use mark-up regulation as part of a generic medicine promotion policy, for example by providing higher remuneration for generic medicines or any other group of products, but this is not commonly practiced.

- Regulating mark-ups in the private sector is probably more complex than in the public sector. Improving efficiency of procurement and distribution in the public sector should be considered as a strategy to lower pharmaceutical costs.

- Regulating mark-ups without adequate enforcement is probably not effective and adequate enforcement in low-income countries appears challenging.

- Mark-ups that include a regressive component with or without fixed fees probably lead to better outcomes that fixed percentage mark-ups through their influence on financial incentives. However, fixed fee mark-ups can dramatically increase the price of otherwise low-cost medicines.

- While banning discounts, rebates and bonuses in the supply chain probably increases transparency in medicine pricing, there is insufficient evidence to say whether it leads to reduced prices.

1. Introduction

Access to medicines is determined by a number of interlinked factors including the availability of safe and effective, quality medicines, a reliable supply system, rational selection and use of medicines, and a functioning health care system. Even when these elements are present, the lack of affordable medicine prices can impede access to essential medicines. The prices of medicines themselves are affected by the manufacturer's selling prices, duties, taxes and mark-ups along the supply chain. Each of these can be addressed separately or compositely in attempts to reduce the prices of medicines and facilitate access to essential medicines.

This review addresses the issue of regulating medicine mark-ups in the supply chain from the manufacturer's selling price to the final patient price with a focus on the situation in low- and middle-income countries (LMICs)[a].

1.1 Definition of the policy

The policy addressed in this review is the regulation of distribution mark-ups in the supply chain of medicines. It thus covers the regulation of wholesale and retail mark-ups as well as considering some aspects of pharmacist remuneration. Discounts and rebates are not specifically covered although reference to them was sought in the reviewed papers. Duties, taxes and other public levies or charges are also not covered although they may also represent substantial add-on costs to the final price of a medicine. It is implied that regulation of mark-ups can lead to lower medicine prices (or at least control them and/or contain costs).

A **mark-up** may be simply defined as the difference between the purchase price (cost price) and selling price of a commodity. A mark-up thus represents the additional charges and costs which are applied in order to cover overhead costs, distribution charges, and a profit and may also be described as the "gross profit". The mark-up may be expressed as a defined, fixed value or as a percentage of the price at which the goods or services were procured (the purchase price) or a combination of the two. Mark-ups are often expressed as a percentage of the purchase price.

$$Percent\ mark-up = \frac{(selling\ price - purchase\ price)}{purchase\ price}\ x\ 100$$

The word **margin** is often used in the context of a mark-up and is sometimes used synonymously with it in the literature and in practice. However, strictly speaking, a margin represents the difference between the purchase price (and variable costs of selling) and the selling price expressed as a percentage of the selling price. It may be alternatively referred to as

[a] Based on The World Bank classification http://data.worldbank.org/about/country-classifications/country-and-lending-groups

the profit margin or gross profit margin – the size of which will depend on the mark-up applied. In this report, the term 'mark-up' is used throughout unless specific reference is intended to be made to the 'margin'.

$$Percent\ margin = \frac{(selling\ price - purchase\ price)}{selling\ price}\ x\ 100$$

Before considering the impact that regulation of mark-ups might have on medicine prices and other aspects of the pharmaceutical sector and the use of medicines, it is prudent to consider the environment in which they are applied so as to appreciate the effects, expected and unexpected, which may occur as a result of regulating them.

1.2 The supply chain

The supply chain is often, although not always, organized separately and operated independently between the private and public health sectors.

1.2.1 Private sector supply chain

The traditional supply chain for medicines in the private sector is illustrated in *Figure 1*, whereby the manufacturer or importer of the medicines sells it on in bulk to a wholesaler / distributor (in this paper the terms 'wholesaler' and 'distributor' are used interchangeably unless specified; see the *Glossary* for distinctions between them) who carries a range of products from multiple manufacturers. The wholesaler then sells smaller quantities to retailers, who are usually a private or public pharmacy but could be general traders, dispensing doctors, or other authorised selling points for medicines. In the case of manufacturers outside the country of sale, there may be an importer or trader(s) acting between the manufacturer and wholesaler, although in some cases the wholesalers do the importation themselves.

The manufacturer's selling price (MSP) usually incorporates various costs and charges including production costs and the profit margin. The 'add-on costs' applied by manufacturers are usually not known and the term 'mark-up' is usually used to refer to the wholesaler–retailer and retailer–patient transactions.

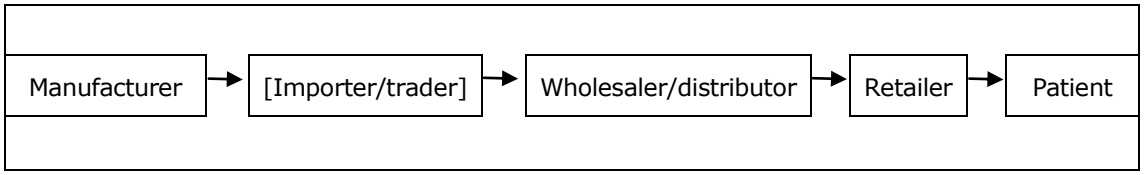

Figure 1. **Traditional supply chain for medicines in the private sector**

This traditional distribution model has been modified in various countries due to prevailing market conditions, pharmaceutical regulation and marketing strategies. Figure 2 provides some examples of alternative supply chain models of which only one

or two may be in operation in a given country or, in some cases, they may co-exist. For example, some manufacturers have dedicated wholesalers or distributors and will not make their products available to other wholesalers. Some wholesalers may carry the full range of available stock (full-line or fully-sorted wholesalers) while others may restrict themselves to certain products or certain manufacturers (short-line wholesalers). In some countries, wholesalers are legally required to be full-line businesses. Full-line wholesalers may need the support of primary stockholders and/or short-line wholesalers to help them efficiently meet the wide inventory that they are expected to carry and distribute. Distribution in geographically challenging situations may also result in multiple wholesaler solutions. Thus, it is possible for some products to pass through a number of wholesalers before reaching the retailer and patient. Some country examples are shown in *Box 1*.

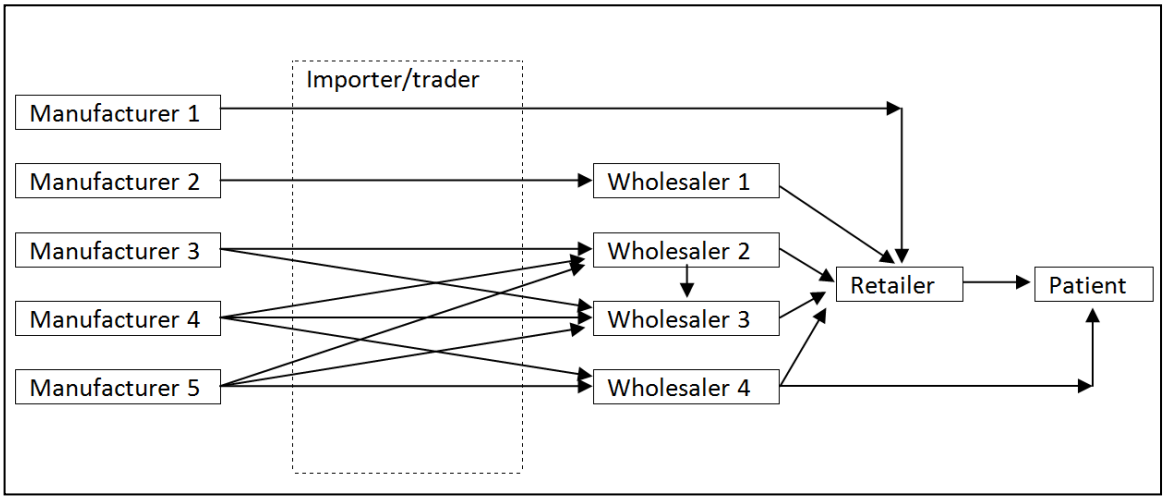

Figure 2. **Examples of supply chain models which may exist in the private sector**

Note to Figure 2 (these are only examples and additional permutations are possible):

- *Manufacturer 1 sells directly to the retailer.*
- *Manufacturer 2 has an exclusive distribution agreement with Wholesaler 1.*
- *Manufacturer 3 does not make products available to all wholesalers.*
- *Manufacturers 4 and 5 are willing to sell to any wholesaler.*
- *Wholesaler 1 is a dedicated short-line wholesaler and carries a restricted product line (from only 1 or a limited number of manufacturers).*
- *Wholesaler 2 may sell on to other wholesalers or on to retailers whereas Wholesaler 3 only sells to retailers and Wholesaler 4 sells to retailers as well as directly to patients.*
- *Retailer may be any dispensing outlet e.g. pharmacy, hospital, dispensing doctor.*

Each of these steps in the distribution chain would incur a mark-up. Horizontal and vertical integration can occur where pharmaceutical and competition laws permit, as companies act to improve efficiency and react to the market environment. Various degrees of market concentration may occur at wholesale or retail level. Manufacturers may supply directly to retailers, particularly hospitals, and may also seek to establish exclusive distribution arrangements with certain wholesalers. Any resulting improvements in efficiency have to be balanced against potential anti-competitive practices that may arise.

The actual mark-up incurred within a distribution transaction can be influenced by commercial practices involving discounts, rebates and other trade schemes. These provide a means of competition between supplier and purchaser and are commonly based on the volume of goods purchased and/or sold, as well as payment terms. Various mechanisms may be used by suppliers of medicinal products to induce their clients (wholesalers or retailers) to purchase and sell on more of their products. These can include cash rebates, volume discounts, bundling or other deals e.g. 10+1 (pay for 10, get 1 free). There may be additional discounts or incentives offered e.g. an extra payment for making sales data available, or early payment discounts. The effect of such mechanisms is to increase the margin of the purchaser, whether wholesaler or retailer, which should be offset to the supplier through improved sales, cash flow or business intelligence. They also decrease transparency of the actual selling cost of a medicine, particularly rebates where the invoiced price does not capture the payment that will be made back to the buyer by the seller.

Consult other texts and reports on pharmaceutical distribution and supply chain dynamics for more detailed description and analysis.

1.2.2 Public sector supply chain

A number of different supply chain models are in operation in the public sector in various countries. The traditional model is usually taken as that of a centralised distribution model (see *Figure 3*). As with the private sector model, the manufacturer may be domestic or international, and may supply through intermediaries such as international procurement agents. Depending on the size of the country and the centralised distribution model, there may be a greater or lesser need for lower level stores.

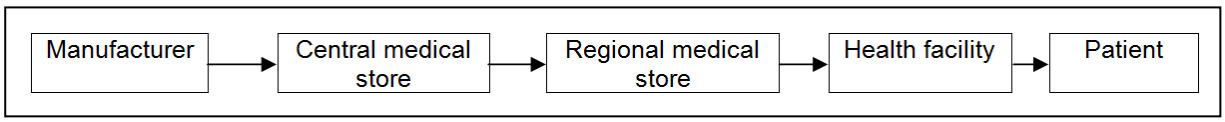

Figure 3. **Traditional centralised supply chain model in the public sector**

In reality, a number of supply chain or distribution models are used in the public sector depending on the country, past experience, procurement practice and the resources available. These include the use of autonomous supply agencies, direct delivery systems, prime vendor systems or fully private supply (*1*). For example, some countries practising centralised public procurement do not have centralised public sector medicine stores but rather opt for direct delivery from manufacturer to district stores or even health centres. In others, a private distributor is contracted to act as wholesaler for the public medicines supply and to distribute medicines to the health facilities. In some cases, combinations of supply chain models may be used depending on the medicines in question. Vaccines or high cost, slow-moving items may be supplied directly to health facilities for example, while other dosage forms go through a centralised distribution system. In decentralised procurement systems it is possible that administrative areas or even individual health facilities obtain their own supplies from manufacturers or private sector suppliers. This is particularly common in the case of hospitals.

Box 1. **Examples of country private sector distribution models**

India: the pharmaceutical distribution sector is fragmented with many layers due to the large country size, national and regional taxation, and pharmaceutical policies. The common model involves domestic manufacturers making their products available through company-owned depots and/or Cost and Freight (CAF) agents or super-stockists (in each case the manufacturer retains ownership of the products; CAF agents only provide logistics services whereas super-stockists will also undertake marketing of the products). They distribute the pharmaceuticals to smaller stockists, then through local wholesalers (sub-stockists) to retailers. However, various distribution actors may be included/excluded depending on local laws, e.g. manufacturers, super-stockists and stockists may supply health institutions and some other retailers directly without going through lower level distributors. At the same time, strong national and local unions of retailers and stockists prevent manufacturers from bypassing the accepted supply chain without their agreement. This also effectively prevents market domination by large stockists. It is estimated that there are about 65,000 stockists operating in India (*2*).

Philippines: originator brand medicines are largely imported. They are warehoused by a large distributor that charges a service fee (rather than taking ownership and charging a trading margin), and also plays the role of exclusive distributor for these products to retailers. Some locally produced branded generics are supplied to the market through the same distributor under exclusive distribution contracts, while others are distributed by the manufacturer itself (or a subsidiary). Other products - domestic and imported -are made available to a large number of wholesalers who may supply other smaller wholesale distributors. Some wholesalers enter into consignment contracts with retailers whereby the former retains ownership of the company's inventory, with the latter only paying for stock that is sold. There are over 4,000 licensed distributors in the Philippines (*3*).

South Africa: traditional pharmaceutical wholesalers have been a strong force in the South African pharmaceutical sector. However, starting in the 1990s, groups of pharmaceutical companies established their own distribution agencies to supply their products while others entered into distribution agreements with independent third-party logistics companies. These changes allowed manufacturers to bypass wholesalers and gain greater control over the supply and marketing of their products as well as increase their margins at the expense of wholesalers. Around the introduction of the pricing regulations in 2004, it was estimated that three large agency distributors controlled around 70% of the distribution market. The pricing regulations prohibited discounts and rebates in the pharmaceutical sector, set a single exit price from manufacturers, and set a fee-for-service logistics fee as compensation for wholesalers or distributors and a dispensing fee for retailers. Licensed pharmaceutical wholesalers and distributors number less than 150[a] (*4,5*).

EU: the past few decades have seen considerable consolidation in the pharmaceutical sector with vertical and horizontal integration to increase market share, control supply chains and increase margins through economies of scale. Price and other regulations in the pharmaceutical sector have contributed to these moves. As a result, large wholesalers are common and while there are over 600 full-line wholesalers in Europe, in most EU countries around half to two thirds of pharmaceutical distribution is provided by three major local wholesalers with a few large transnational wholesalers also in existence. In countries where laws permit, vertical integration has occurred e.g. in the UK, Boots plc. combines manufacturing (of 'own brand' medicines), wholesaling and retailing activities although competition laws usually limit market dominance. Parallel importation of medicines between EU states has added a further aspect to pharmaceutical distribution activities. In some countries (e.g. France and Italy) wholesalers are legally obliged to be full-line operators (*6*, *7,8*).

[a] http://www.mccza.com

1.2.3 Interactions between public and private supply chains

Public and private supply chains do not usually operate in isolation, particularly with respect to the supply from manufacturers. Figure 4 shows how public and private sector supply systems could interact. It is only an example based on traditional models. Other models also exist, for example, where private retailers can purchase supplies from the public supply chain, or where public patients obtain their medicines from private retailers.

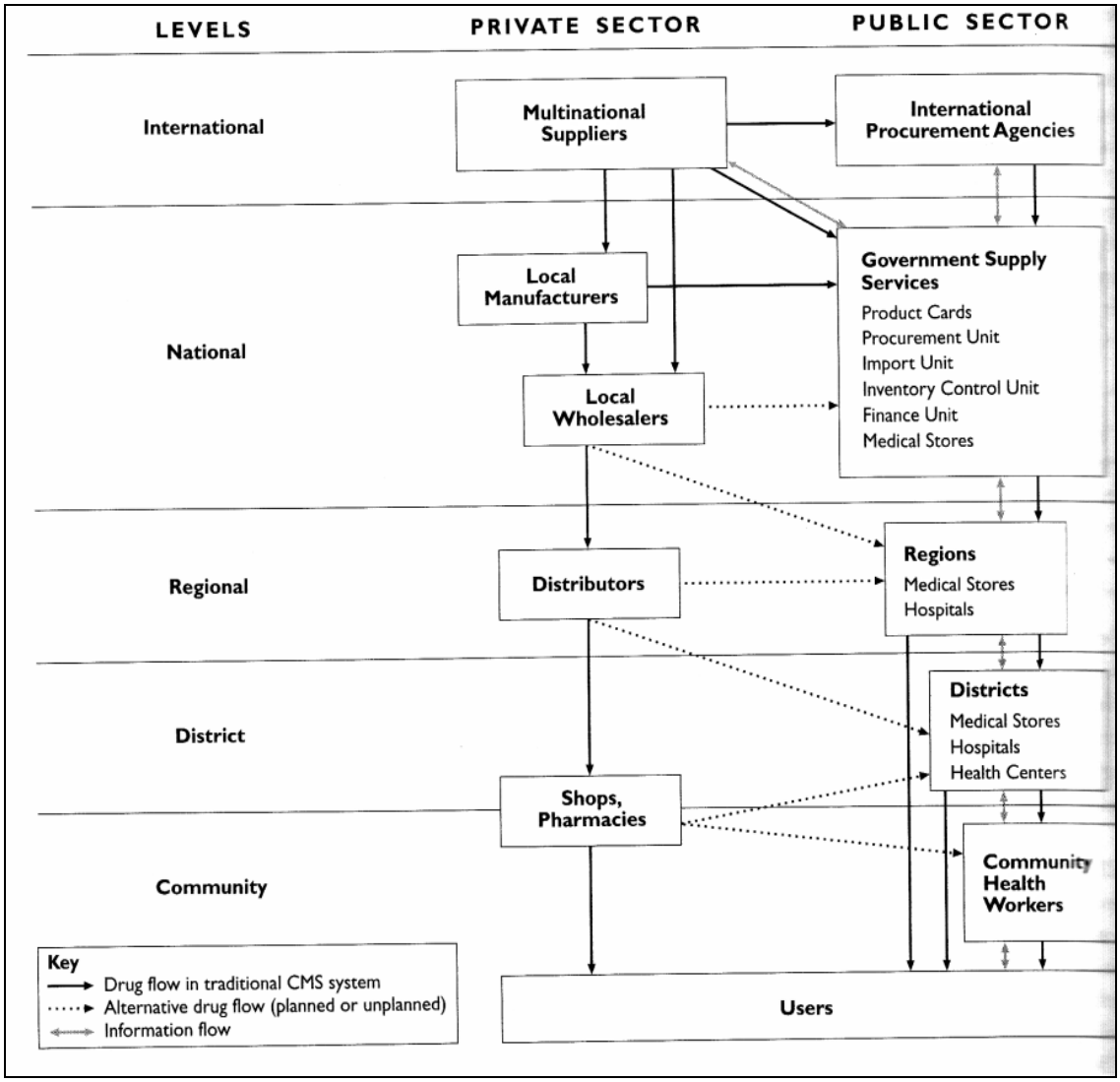

Figure 4. **Traditional parallel public and private sector medicine distribution systems showing potential interactions** (*9*)

This paper will concentrate on wholesale and retail mark-up regulation. However, as shown in Figure 2, it should not be assumed that there is a single wholesale or retail mark-up if there are multiple stages in the supply chain. Some countries set or regulate manufacturer selling prices as part of price regulation but that is beyond the scope of this paper. It should also be borne in mind that importers, traders or other procurement agencies may apply mark-ups independently of wholesalers and they may need to be taken into account where price regulation is envisaged.

2. Objectives

The objectives of this review is to describe, analyse and discuss mark-up regulations and any known evidence of their impact on medicine prices, with a particular focus on low- and middle-income countries.

3. Methodology

A search of the literature was performed to determine the evidence base of experience with regulating mark-ups on medicines and the impact these have on medicine prices in low and middle-income countries.

Searches were performed using PubMed, EconLit and Google.

PubMed

The search strategy involved a combination of four search steps which individually addressed the policy, the supply chain, pharmaceuticals and developing countries. These were combined as follows: *policy search* AND *supply chain search* AND *pharmaceuticals search* AND *developing country* . The combined search yielded 564 articles. The titles and, if necessary, abstracts were scanned to determine the relevance of these publications which reduced the number to 67 articles. Further scanning of the full text of the remaining list left 31 relevant publications.

EconLit

Similar to the PubMed search, a stepwise approach was taken combining searches for policy, pharmaceuticals and developing countries, limited by descriptors, according to: *policy search* AND *pharmaceuticals search* AND *developing country search.* The combined EconLit search yielded 37 hits which reduced to seven after determining relevance by checking titles and abstracts.

Internet

The Google search engine was used to search the internet for relevant literature but due to the breadth of the topic and the range of literature indexed, an efficient search strategy was not easily identified. Broad search strategies e.g. 'pharmaceutical AND pricing AND policy' yielded too many hits to be effective and largely identified articles related to high-income countries. Including the term 'markup OR mark-up' was too restrictive other than for full-text searches. Due to the difficulties experienced, a multiple search approach was used, substituting search terms into various search strategies in an attempt to identify additional articles. The search terms used were: *markup, mark-up, margin, "developing countries", "pharmaceutical policy", wholesale, retail, pharmaceutical, drug, medicine*. Due to the number of hits received on many searches, it was not possible to scan all articles. Where more than 500 hits were found, the first 100 were assessed for relevance. Newspaper articles were excluded unless found to have specific useful information.

Other methods

To complement the above searches, additional methods were employed to identify grey literature and publications not indexed by PubMed or EconLit:

- Purposive searching of pharmaceutical policy papers and publications and their reference lists.
- E-Drug/E-Med messages.
- WHO/HAI medicine price database[a].
- Personal approach to professionals in the field.

A wide range of articles and papers were found. For this paper, those specifying actual mark-ups for wholesale and retail stages or reflecting on a policy of regulating mark-ups or margins were focused on.

See Appendix 1 for the search terms used

Three country case studies are presented as examples of how low- or middle-income countries have approached the regulation of distribution mark-ups. The countries were selected after discussion with members of the WHO/HAI Pricing Policy Working Group and taking into consideration that they should:

- be middle- or low-income economies;
- have recently taken action to implement or change mark-up regulation;
- have reliable literature about their mark-up regulation mechanism.

The countries chosen were Albania and South Africa, both upper-middle-income countries, and Mali, a low-income country. Albania had continued to use fixed percentage mark-ups at wholesale and retail level but was starting to take action to control prescription/dispensing of high value pharmaceuticals. South Africa was selected due to its tribulations in implementing wholesale reform of medicine prices which it was felt would provide valuable lessons to other countries considering similar action. Mali did not formally regulate mark-ups but provided an example of a novel approach to price regulation of a selected group of essential medicines in a low-income country.

[a] http://www.haiweb.org/medicineprices/

4. Review of the evidence

There is a general lack of information on the implementation and/or effects of regulation of wholesale and retail mark-ups in the medicine supply chain of low- and middle-income countries (LMICs) in the formal biomedical literature. This is probably due to the fact that this form of intervention is usually implemented by government agencies who do not usually publish their actions, or any assessment of them, in the academic journals. Some literature is available which describes the use of mark-ups as a pharmaceutical policy or medicine pricing intervention but limitations include it being either descriptive in nature and/or used in combination with other policy interventions rather than as a sole measure.

The literature review is presented with an initial overview of work discussing the policy of regulation of mark-ups in general. This is followed with more specific analysis of data which is available to address questions as to the magnitude of regulated distribution mark-ups in various countries, strategies used to regulate mark-ups, evidence for their efficacy in lowering medicine prices, enforcement issues and general guidance in applying regulated mark-ups as part of a policy intervention in medicine pricing.

4.1 General overview

Price regulation in the distribution chain is not a new topic and is practiced in many countries. It has been suggested that distribution mark-ups (including both wholesale and retail activities) should be regulated since they can represent more than 40% of the price ultimately paid by the user or patient (*10*). Experience from medicine price surveys undertaken using the WHO/HAI methodology[a] supports this with, in some extreme cases, retail mark-ups accounting for up to 90% of the final price (*11*). However, in many countries the manufacturer's selling price is the major contributor to the final price (WHO/HAI data).

Enemark and colleagues (*12*) have argued that prices could be set at actual cost, cost plus a mark-up (percentage or flat fee), or simply as a flat rate per prescription or medicine item. However, these need to be considered in more detail. Five basic options for the regulation of mark-ups in the distribution chain have been proposed in the past (*9*, *13*, *14*, *15*) but should not be seen as being comprehensive in terms of the strategies which might be employed:

[a] http://haiweb.org/medicineprices/

Cost + fixed percentage:	All medicines receive the same mark-up as a percentage of the cost price.
Cost + declining percentage:	More costly medicines attract lower percentage mark-ups
Cost + fixed dispensing fee:	Pharmacist charges the wholesale cost plus an additional fixed or flat fee.
Cost + differential dispensing fee:	Generic or limited list medicines get a higher dispensing fee to increase the incentive to dispense them.
Maximum allowable price:	The sale price or reimbursement level is fixed for the generic equivalents of certain drugs or for therapeutic categories.

Rietveld & Haaijer-Ruskamp (*10*) took the view that the regulation of wholesale and retail mark-ups should be separated. They suggested that **wholesale** mark-ups can be limited either by setting:

- a maximum allowable mark-up or margin; or
- a maximum price for resale; or
- a combination of these strategies.

The form of regulation used for **retail** sales can be either product-oriented or patient-oriented.

Product-oriented approaches would involve the regulation of mark-ups by:

- applying a fixed percentage mark-up; or
- setting a maximum mark-up; or
- using regressive (also digressive or degressive) mark-ups.

Patient-oriented approaches would involve:

- Capitation systems – where the retailer is paid a fixed fee per patient per year; or
- fixed fees per prescription item – where the retailer receives a fixed amount prescription item dispensed; or
- a combination of the above.

In practice, it is also possible to combine both product-oriented and patient-oriented approaches so as to balance the incentives and also allow the wholesaler or retailer to make sufficient profit to be viable.

Country experiences indicate that there are a number of variations around these themes, with strategies including combinations of fixed fees and percentage mark-ups (regressive or fixed) at either wholesale or retail level, sometimes with additional dispensing fees. Where regressive mark-ups are applied, they could be in the form of fixed fees or percentages and could have few or many thresholds or levels of capping. Three examples are given in Table 1. In the examples shown, Syria employs a regressive percentage, Australia a combination of regressive percentages plus fixed fees plus a dispensing fee, and New Zealand a limited progressive percentage mark-up plus a dispensing fee.

Table 1. **Examples from three countries of different retail mark-up strategies**

Syria (*16*)		**Australia (*17*)**		**New Zealand (*7*)**	
Purchase price (SYP)	**Pharmacist's mark-up†**	**Purchase price (AUD)**	**Pharmacist's mark-up***	**Purchase price (NZD)**	**Pharmacist's mark-up***
1-40	30%	≤ 30	15%	< 150	4%
41-80	20%	30-45	A$4.50	≥ 150	5%
81-200	15%	45-180	10%		
201-500	10%	180-450	A$18.00		
≥501	8%	450-1750	4%		
		>1750	A$70.00		

†*Incurred sequentially i.e. first SYP40 at 30%, next SYP41-80 at 20%, etc.*
**Pharmacists also receive a fixed dispensing fee*

A number of papers have examined price regulation, including regulation of mark-ups, in high-income countries (HICs).

Appendix 2 provides an overview of mark-up regulatory strategies in the OECD (*17*). These will be considered in more detail below. Ess and colleagues (*18*) noted that many European countries have defined profit margins for wholesalers and retailers as part of cost-containment measures. They further noted that other measures such as parallel trade were used in some countries. These could lead to lower procurement costs for wholesalers and either lower selling prices for the wholesaler/retailer, if mark-ups are regulated, or increased profits where mark-ups are not regulated.

4.2 Rationale behind distribution mark-up regulatory strategies

While price regulation is normally aimed at reducing medicine prices and cost containment, it is important to recognise that distribution mark-ups are not only determinants of the selling price of medicines. They also contribute to the creation of incentives and disincentives throughout the supply chain, including the point of dispensing or purchase. They could thus operate independently or as part of a pricing policy which also regulates producer prices or final selling prices. They may also be used in relation to local industrial policies, perhaps favouring domestic manufacturers e.g. Luxembourg applies lower wholesale margins to products originating from within its borders (*6*).

The different mark-up regulation strategies listed previously therefore represent attempts to address the incentives and disincentives in medicine supply that each component introduces (*9*, *10*, *13*). For example, fixed percentage mark-ups may reduce prices of specific medicines but will also tend to encourage stocking and the sale of higher cost products rather than lower cost generic and/or essential medicines. The presence of discounts or trade schemes between players in the distribution chain can also lead to increased profits without patients benefiting from lower prices. Regressive mark-ups in which higher cost items attract lower mark-ups are one method to counter the incentive to sell higher cost products, while patient-oriented mechanisms attempt to separate the remuneration for dispensing from the cost of the product altogether. Fixed dispensing fees thus create incentives for dispensing lower cost medicines while at the same time lowering inventory costs, but also create an incentive for dispensing more medicines (since each item attracts a fee). The beneficial effects of fixed fees can be negated when combined with fixed percentage mark-ups depending on their relative magnitude, and fixed fees can disproportionately increase the price of low value items.

A summary of advantages/limitations and incentives/disincentives related to the various strategies are presented in Table 2 and examples of strategies are presented in Appendix 3.

4.3 How widespread is the use of mark-up regulation?

In HICs in Europe, mark-ups are commonly regulated. This is usually part of a comprehensive pricing strategy related to the reimbursement of costs of medicines under a national health service or insurance system (*5*, *18*, *19*, *20*). Such systems usually also involve the control or setting of either manufacturer/importer selling prices or the final retail selling price.

The Prescription Price and Reimbursement Information (PPRI)[a] project reported on price regulation in 27 European countries (*21*) and found that in 24 of them prices of reimbursed outpatient medicines were regulated, in most cases incorporating some form of mark-up or margin regulation. In the three countries with free pricing - Denmark, Germany and Malta - only in Malta was the price not regulated at all in the private sector. The United States of America is a rare example of a high-income country that does not regulate mark-ups or indeed medicine prices at national level. The situation in low and middle-income countries is more difficult to determine where public health insurance is less developed and the role of payers in determining prices less clear.

[a] http://ppri.oebig.at

Table 2. **Advantages and limitations of mark-up remuneration strategies**

Remuneration/ mark-up (cost price +)	**Advantages / incentives**	**Limitations / disincentives**
Fixed fee	• No/reduced incentive to sell higher value items • Relatively easy to enforce	• No incentive to sell lower cost items • Adds significantly to the patient price of low-cost medicines
Regressive flat fee/amount	• Reduces incentive to dispense high cost medicines	• Reduces incentive to carry high value stock • Adds significantly to the patient price of low-cost medicines
Fixed percentage	• Relatively simple to implement and enforce	• Disincentive to sell lower cost items • Encourage stocking and sale of more expensive items
Regressive percentage	• Easy to implement • Reduces incentive to dispense high cost medicines	• High cost items may still attract large value mark-ups • May not create incentive to dispense less expensive items
Differential percentage or fixed fee	• Incentives can be created for particular groups of medicines e.g. EML, generics	• More complex to implement and enforce
Fixed maximum fee / percentage	• Incentive for competition	• May lead to reduced service quality or range of products in drive to lower costs • Disincentive to sell lower cost items if fixed percentage and inadequate competition or room to reduce costs • Incentives exist for retailers to sell more expensive drugs
Combined mark-up to be divided following negotiation	• Reduces regulation	• Retailers may bypass wholesalers and increase margins/mark-up
Capitation fees	• No link to the sale or cost of the medicines • No incentive to sell high cost items	• Sophisticated administration systems required
Capping of mark-ups	• Reduces incentive to dispense very high cost items	
Combinations of above	• Combinations of above	• Combinations of above

Contrary to the knowledge about mark-up regulation in HICs, there is little systematic literature of the situation in LMICs. An impression of the situation can be obtained by considering a number of disparate sources but the majority of the information is self-reported and not collected from representative samples.

A survey of Latin American countries found a variety of approaches to pricing of pharmaceuticals from free pricing through to fixed prices (*22*). Ecuador, Honduras, Panama and Paraguay used comprehensive price control with the former three stipulating wholesaler and pharmacy mark-ups or margins, whereas the remaining countries either used some form of intermediate control e.g. monitoring prices and regulating price increases, or allowed prices to be set by the market.

Results from the WHO Level 1 Indicator Survey of country pharmaceutical situations in 2007 showed that around 65% of 156 respondent countries reported regulating public sector wholesale mark-ups, compared to 75% in the case of the private sector (*23*).

Table 3. **Proportion of countries reporting presence of pricing policies or mark-up regulations in WHO Level I Indicator Survey (*23*)** (based on 2007 data)

Countries (n=156)	Pricing policy	Max wholesale mark-up	Max retail mark-up
Public sector	65%	65%	68%
Private sector	60%	75%	81%
NGO sector	39%	52%	54%

Data is calculated as % of responses given to each question.

The application of maximum retail mark-ups in the public and private sectors appears to follow a similar pattern, with 68% and 81% of countries regulating public and private sector retail mark-ups respectively. When this information is aggregated according to the income level of the country, the data suggests that where mark-ups are regulated, both wholesale and retail mark-ups are subject to regulations in the public sector; in the private sector, retail mark-ups are more likely to be regulated than wholesale mark-ups (*5).* However, it is difficult to make sound conclusions about the application of mark-up regulations from this WHO indicator data which should be interpreted with caution due to the self-reported nature of the methodology, the incomplete nature of the data, and the low response rate to questions about maximum mark-ups. Observations from WHO/HAI pricing surveys tend not to support conclusions drawn from the indicator surveys (*see Table 4* and *Appendix 4*) but it is not possible to say which is the more reliable or representative data, especially since the regulatory status of mark-ups was not systematically collected in the WHO/HAI surveys.

Subsequent to, and using a similar methodology to the WHO Level 1 indicator surveys, pharmaceutical profiles have been prepared for countries in the Southern African Development Community states[a]. Four of fourteen countries reported regulating wholesale mark-ups and six reported a maximum retail mark-up (*Table 5*). When compared to the WHO Level 1 indicator surveys, this shows that there may be distinct regional variations masked within the aggregated data.

4.4 Magnitude of regulated mark-ups

The magnitude of wholesale and retail mark-ups in HICs has been the subject of past work (*13*, *18*, *24*) (*see Appendices 7* and *8*) but the most recent reliable information is available from the Pharmaceutical Pricing and Reimbursement project (PPRI)[b] (*21)* with an associated Organisation for Economic Co-operation and Development (OECD) report on pharmaceutical pricing policies (*6*). Information from LMICs is sparse and has not been collected systematically. The WHO/HAI medicine pricing surveys[c] provide most of what is known but this is based on an unrepresentative sample of countries, and the data is derived from very few data points i.e. a small number of medicines in each country.

High-income countries

OECD data (*6*) suggests that mark-ups in HICs vary widely (*see Appendix 2*):

- Wholesale: 2% – 21% (some are capped or utilise fixed amounts).
- Retail: 4% – 50% (with price caps, combinations with fixed amounts and dispensing fees, differential mark-ups according to category of medicines (reimbursed, generic, prescription-only).

Data from the PPRI project (*21*) found that 21 of the 27 participating European countries regulated wholesaler mark-ups and pharmacy margins were controlled in all 27 countries, although not always through statutory mark-ups. There were many variations in both mechanism and value of the mark-ups. In some cases all medicines were covered by the mark-up regulations; in others non-reimbursed OTC or hospital-only medicines were excluded or had differential mark-ups (*20*, *21*).

[a] http://www.who.int/medicines/areas/coordination/coordination_assessment
[b] http://ppri.oebig.at
[c] http://www.haiweb.org/medicineprices

Table 4. **Available data from WHO/HAI surveys and other sources on the magnitude of regulated mark-ups in the public and private sectors**

WHO Region (no. countries with data)	**Range (n) regulated public wholesale mark-up**	**Range (n) regulated public retail mark-up**	**Range (n) regulated private wholesale mark-up**	**Range (n) regulated private retail mark-up**
AFRO (n=19)	20-50% (2)	30 (1)	27.5% (1)	5-76%[1] (2)
EMRO (n=12)	10% (2)	0-20% (3)	2-35% (11)	8-42.9%[1] (11)
EURO (n=8)	15% (1)	15% (1)	25% (1)	30-35% (2)
PAHO (n=12)	-	25% (1)	4-30% (4)	25-30% (3)
SEARO (n=5)	-	-	8-10% (1)	16-20% (1)
WPRO (n=5)	-	30% (1)	-	-

Where more than one data point exists for a country, the most recent was used.
[1]Some countries use regressive mark-ups schemes.

Table 5. **Indicators on medicines pricing from the assessment of the pharmaceutical situation in SADC member states[a].**

	Legal or regulatory provisions exist for setting:						
	MSP	Max wholesale mark-up	Max retail mark-up	Max retail price	Provisions vary for different medicine types	Government has active retail price monitoring	Retail medicine price info is publicly accessible
Angola	-	✓	✓	✓	×	×	×
Botswana	×	×	×	×	NA	×	NA
DRC	✓	✓	✓	×	×	×	×
Lesotho	×	×	×	×	NA	×	NA
Malawi	×	×	×	×	NA	×	NA
Mauritius	✓	✓	✓	✓	×	✓	×
Mozambique	✓	✓	✓	✓	×	✓	✓
Namibia	×	×	×	×	NA	×	NA
Seychelles	×	×	✓	×	×	×	×
South Africa	×	×	✓	×	✓	✓	✓
Swaziland	×	×	×	×	NA	×	NA
Tanzania	×	×	×	×	NA	×	NA
Zambia	×	×	×	×	NA	×	NA
Zimbabwe	×	×	×	×	NA	×	NA

Key: *MSP – manufacturer's selling price; DRC – Democratic Republic of Congo; NA – Not applicable*

[a] Data derived from country profiles available from http://www.who.int/medicines/areas/coordination/coordination_assessment

The wholesale and retail mark-ups or margins were not usually set independently, but rather as part of an integrated pricing strategy which could incorporate profit controls or other measures of determining a final price with a total mark-up split between retailers and wholesalers (*5*, *19*, *20*, *21*).

Low- and middle-income countries

Evidence from the WHO/HAI surveys and other literature available (*see Table 5* and *Appendix 4*) suggests a variety in regulated mark-ups in LMICs. Across both public and private sectors, wholesale data suggest ranges between 10% – 35% with retail mark-ups ranging between 0% and 76%. Variations result from country factors, whether public or private sector and whether there are any differential mark-ups depending on the class or type of medicine. Cameron and colleagues (2009) in a secondary analysis of the WHO/HAI data reported total cumulative mark-ups (which includes all mark-ups from MSP through to final patient price) ranging from 17% – 84% in the public sector and 11% – 6,894% in the private sector.

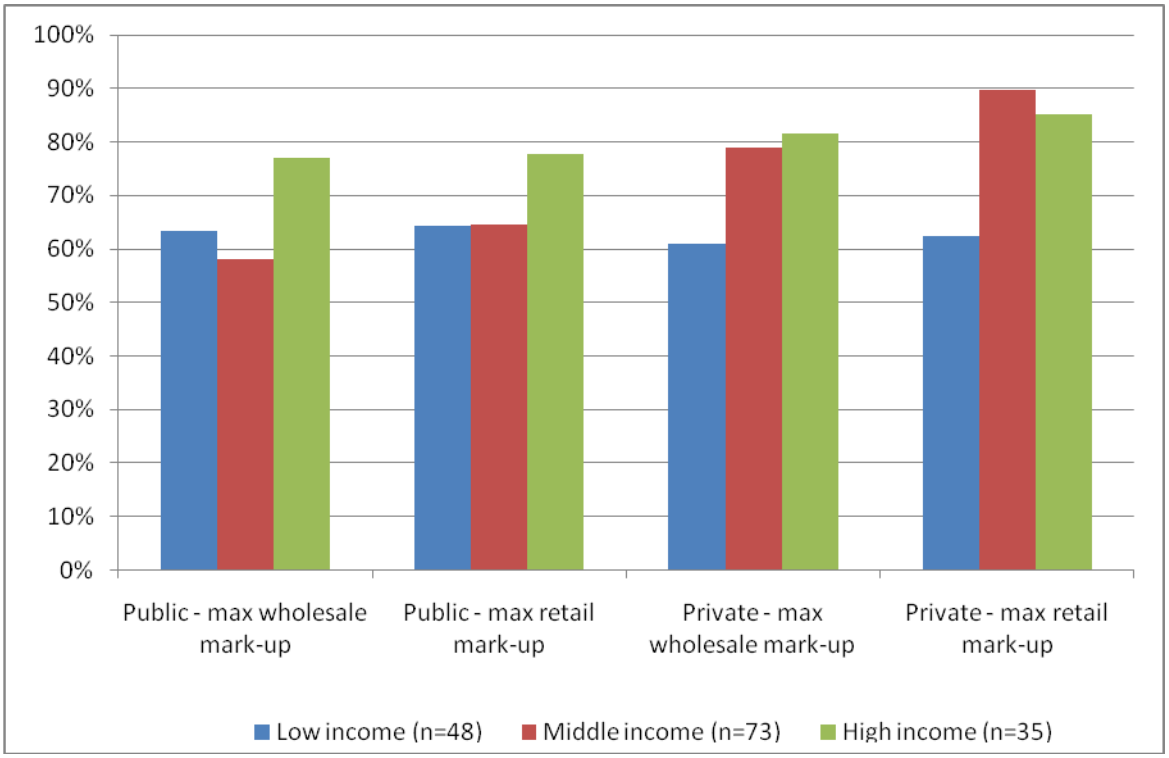

Figure 5. **Reported medicines pricing policies and regulated maximum wholesale and retail mark-ups in the public and private sectors (*23*).**

Of particular interest from the WHO/HAI data, while bearing in mind its limitations, is that relatively few countries implement regressive or differential mark-ups schedules, and usually only in the private sector. The countries concerned, namely India, Iran, South Africa, Syria, Tunisia and the UAE, were all middle or high-income economies. Where regressive scales exist, the difference between the upper and lower mark-up may also be quite large in some countries but narrow in others e.g. retail private sector in Syria 8% – 30%, but in Tunisia 31.6% – 42.9%.

Looking at mark-up magnitude in isolation of the country size, level of development and urbanisation, health system structure, procurement price and other factors which affect distribution costs, is likely to be a misleading and unfruitful exercise. While the ranges of regulated mark-ups provide some measure of comparison, it should be recognised that there is no simple level or range of what constitutes a reasonable wholesale or retail mark-up and that mark-ups should be seen as incentive tools in addition to any direct affect they may have on medicine prices and, by extension, availability.

Importers and other agents

Importers and other agents or agencies responsible for importing medicines into a country can represent another source of significant mark-ups for medicines early in the supply and pricing chain. These are perhaps particularly relevant in low-income countries (LICs) which do not have established domestic pharmaceutical manufacturers and import most, in some cases all, of their pharmaceutical supplies. In Uganda, importers were found to apply mark-ups ranging from 20%-70% on antimalarial medicines (*11*, *23*) whereas in Sri Lanka, an importer mark-up of 25% contributed almost as much as the wholesale and retail mark-ups combined to the final patient price (WHO/HAI survey database[a])(*26*). Since these mark-ups are engaged early in the supply chain, the size of subsequent percentage-based mark-ups is increased and the cumulative mark-ups to the final selling price can be considerable. Distributors also add to cumulative mark-up and can have a larger effect than realised when multiple distributors and/or wholesalers are involved. In the Philippines, multiple distribution steps were a common feature of the supply chain for medicines surveyed as part of a price component study, particularly for generic medicines (*2*).

Little of the literature explicitly mentioned control or regulation of importer mark-ups. In some HICs this is implicitly covered by the price regulation or reimbursement mechanism in place. LMICs that regulate public procurement prices may also explicitly or implicitly regulate importer mark-ups. Chad and Ghana, for example, regulate the mark-up for central medical stores as the importer, with Ghana applying larger mark-ups to imported pharmaceuticals (*see Appendix 4*). In practice, for policy-makers there is little or no practical difference when regulating importers and distributors compared to regulating wholesalers and retailers. But if importers are excluded from the regulation process, substantial loopholes are left through which medicine prices and margins can be manipulated. To address such concerns, a fixed distribution margin can be set which is then split between the parties involved through regulation or negotiation – such a mechanism was employed in South Africa as part of its price regulation (*4*, *27*, *28*).

4.5 Public vs. private sector regulation

For LMICs, the data available is scant and unreliable (*see Appendix 4*). While there are some differences between the mark-ups applied between public and private sectors, very few countries appear to actually regulate mark-ups in both public and private sectors so care should be exercised in interpretation of this data.

[a] http://www.haiweb.org/MedPriceDatabase/

Public sector mark-ups range mostly between 10% – 20% for wholesalers and 0% – 30% for retailers but there are few data points on which to base these observations. There is somewhat more data for the private sector, where regulated wholesale mark-ups range from 2% – 35% and between 8% - 76% for the retail sector. It should be noted that in some countries there are variations to allow for locally produced, as opposed to imported products, originator brand versus generic medicines, and additional mark-ups in some cases for importers (sometimes included in the wholesale mark-up) or regional stores and distribution steps.

It can be difficult to compare mark-up regulation in the public sector between countries since different supply models may operate: they may operate wholly by tender; rely mostly on imported medicines; procure from local wholesalers; or require patients to purchase their medicines from private retailers. Some public sector operations may be run on a commercial basis while others are not. Where public sector medicines are procured at low-cost, higher mark-ups may be justified to cover distribution and holding costs.

In high-income markets, price regulation (where it exists), often focuses on publicly reimbursed medicines which are sold through public or private retail outlets. Private sector sales to private clients are often not regulated but generally form a much smaller segment of the market. Sales of over-the-counter (OTC) medicines may also be exempted from regulation. In France, for example, medicines reimbursed under the national social health insurance have their prices regulated, but there is free pricing and price competition for pharmaceuticals which are not reimbursed, those approved for hospital use and over-the-counter medicines (*21*). In some countries, prices of non-reimbursed medicine prices are also set but receive a differential mark-up compared to reimbursed products. The OECD report (*6*) and PPRI data[a] can be consulted for further details.

4.6 Selective mark-up regulation

It is possible to introduce flexibilities in mark-up regulations to make allowances for the type of product and/or its price or other variables. Thus it is possible to have separate strategies for originator brand and generic medicines, medicines on the national essential medicines list and those not on the list, or have some form of regressive mark-ups whereby higher cost products receive lower mark-ups and thus create or influence incentives within the supply chain. Regressive mark-ups can have a differential impact on originator brand and generic medicines where these are marketed at different prices.

While some countries have regulated mark-ups based on the patent or trade mark status of a product, e.g. Indonesia (*29*), this is not generally practiced in HICs. While historically France has used distribution margins as one mechanism to promote the uptake of generic medicines (*30*), none of the European countries in the PPRI project (*21*) applied differential mark-ups between products based on their patent status although particularly expensive medicines (more likely to be originator brands) received lower mark-ups in regressive mechanisms. This is not to say that HICs do not adopt different regulatory strategy with regard to the prices of originator brand and generic medicines. They may often do so, since innovative products do not lend themselves to internal reference pricing or other price regulations which rely on therapeutic competition between similar products. The PPRI country profiles can be consulted for such information[b].

[a] http://ppri.oebig.at
[b] http://ppri.oebig.at

In some countries such as Latvia, different mark-ups were applied to reimbursable and non-reimbursable medicines. These result in lower retail prices for reimbursed products, and lower co-payments for patients with the effect of reducing pharmaceutical expenditure for the third-party payer. Other countries applied selective regulation, regulating the mark-ups on reimbursable medicines but allowing private sales to be freely priced e.g. France (*21*). This again allows expenditure within the national health system to be controlled but leaves market forces to operate in sales outside of the reimbursement mechanism. In Luxembourg, pharmaceuticals which are imported and those originating from Belgium or Luxembourg are treated differently in mark-up regulation, with the latter attracting lower mark-ups. This presumably increases their market share within the national reimbursement system and is a form of promoting the interests of local industry.

Examples of differential or selective mark-up regulation in LMICs are sparse. In India, a select group of medicines, including mostly essential medicines, are 'scheduled' and subject to price regulation (*31*, *32*). The pricing formula incorporates the mark-ups of wholesalers and retailers in the maximum retail price that is determined. This results in lower average margins on these medicines, with the aim of increasing financial access to them. The example of Indonesia (published in 1989 so dated) has been cited above where mark-ups for originator brands were lower than those for generic products (*29*). This allows for higher return on lower cost generics. In Albania, hospital-only medicines are procured centrally or by each hospital (by tender or negotiation) and are then provided free of charge to patients and the mark-ups (if any) are not subject to regulation. Mali is a rare example of a low-income country with a selective pricing policy in which 107 specified essential medicines have their prices regulated in the private sector leaving free pricing on the remainder (*33*). However, mark-ups are not explicitly regulated in this mechanism.

Medicines may be grouped according to patent status (originator brand, branded generic, generic), innovation, country of manufacture, reimbursement status, presence on an essential medicines list or other positive list. Mark-up regulations may address these individually or as particular groups, as determined by competing health and industrial priorities and policies and the pricing policy. Authorities intending to implement regulation of mark-ups should consider to what degree differentiation or selective application of regulation needs to be made. There are risks to such strategies, particularly where the mark-up allowed on the regulated products is set at an unprofitable level. Manufacturers may shift production and sales to more profitable lines and the availability of essential medicines may be adversely affected as has been described for China (*34*, *35*, *36*) and Mali (*33*). Indeed, supply chain stakeholders may find ways to distort selective mechanisms to their advantage so they should be considered as part of a comprehensive strategy and medicines policy which also addresses advertising of medicines and other aspects of the pharmaceutical market.

4.7 Other add-ons in the supply chain

While this paper concentrates on wholesale and retail mark-ups, there are other add-on costs which may be encountered in the supply chain which may be open to regulation. These include:

- Import duties and tariffs
- Miscellaneous government charges e.g. pharmacists' fund, standards organisation
- Taxes, whether local, regional or national (including GST and VAT)

These topics are beyond the scope of this paper. However, as components of the final price they should be considered in pricing analysis and can be used to create incentives e.g. reduced tariffs or taxes on essential medicines can influence supply which may affect availability, affordability, equity and appropriate use of medicines.

4.8 Discounts, rebates and trade schemes

Discounts, rebates and trade schemes can contribute to a lack of transparency in pricing and some countries have chosen to regulate them to minimise abuse (*37*, *38*). Sales incentives may also lead to irrational use of medicines, for example where Philippines retailers receive 'pin payments' for promoting the sale of specific products (*3*). Discounts and rebates may be seen as unfair, since they are often applied asymmetrically and it is often those who are most disadvantaged who end up paying higher prices: smaller retailers serving poorer populations would be considered less likely to receive or pass on volume discounts from wholesalers. In the EU, discounts between manufacturers, wholesalers and pharmacists are legal in many member states (*21*, *39*) (*see Appendix 9*). However, there is little published evidence of the scale or magnitude of rebates and discounts in LMICs, although they are generally assumed to be present in the private sector. From the literature search, they were mentioned in studies of pricing in India (*32*), Kenya (*15*), the Philippines (*3*), and South Africa (*4*, *5*, *15*, *40*) although Waning and colleagues (*41*) found no evidence of bundling or rebates by wholesalers in Kyrgyzstan. Lack of transparency in the granting of discounts between various stakeholders as well as to the public was one of the reasons for introducing price regulation in South Africa (*27*), however, there was no evidence in the literature reviewed that regulating discounts and rebates leads to lower prices.

4.9 Approaches in regulating wholesale and retail mark-ups

It is clear that in HICs there are a wide range of options available in the regulation of mark-ups for wholesalers and retailers that may be used individually or in combination (*7*, *21*). Around one-third of countries use fixed percentage mark-ups for wholesalers (12 out of 36) and retailers (10 out of 36), which may be capped at a maximum value (*see Figure 6* and *Appendices 2*, *7*

and *8*). Fixed fees for wholesalers and retailers (5 and 12 countries respectively) and regressive percentage mark-ups (12 and 16 respectively), alone or in combination, are also used. In some cases, different categories of medicines may incur different fixed fees or be subject to different scales of regressive percentage mark-ups. Dispensing fees for pharmacists are employed in 15 of the 36 countries.

Information from LMICs is limited and has not been systematically collected. Largely anecdotal evidence was collected by Levison (*15*), the WHO/HAI surveys provide some information, and data of varying quality and age is available from the literature (*see Appendix 4 for a summary of data on wholesale and retail mark-ups in LMIC identified in the literature).* Only 25 LMICs were found to regulate one or more distribution mark-up. Where data is available for LICs (n=5), all appear to make use of fixed mark-ups. This approach is also common in the MICs with only 5 of 20 MICs (Iran, Lebanon, Syria, South Africa, Tunisia) using regressive mark-ups and/or fixed fees.

It is worth noting that within these examples, India sets the maximum retail price for selected medicines (scheduled medicines) using a mechanism in which there are implicit mark-ups for wholesalers (8%) and retailers (16%) (*31*, *42*). Others have described these as 'minimum' values (*32*). Prior to 2000, China imposed statutory wholesale and retail mark-ups of 15% but these were found to create incentives for the sale of higher priced medicines (*34*, *35*, *36*) and subsequent amendments to the pricing structures over the past two decades have moved to more comprehensive regulation rather than regulating mark-ups (*35*, *36*, *43*, *44*).

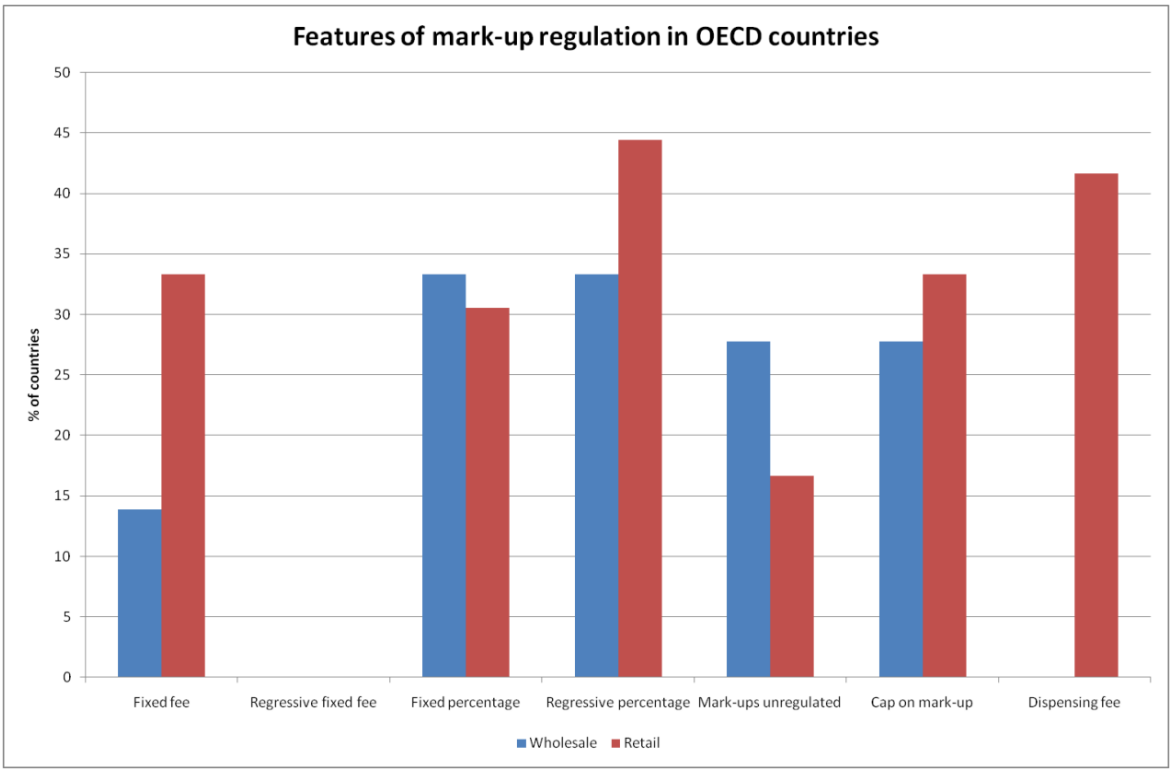

Figure 6. **Features of mark-up regulation in OECD countries (*6*).**

Only Indonesia, Iran and South Africa mention prescription or dispensing fees although this information has not been systematically collected in surveys using the WHO/HAI methodology and other publications, and it is possible that other countries among those listed also employ this mechanism. Such fixed fees remove the incentive to dispense more costly items by breaking the link between pharmacy profit and the price of a medicine. It is possible to pay higher reimbursements or fixed fees for generic medicines or any other group of products, to increase the financial incentive to dispense these items but this does not appear to be commonly practiced in either OECD countries or the three countries identified in the literature search. Fixed fees can be combined with regressive percentages to obtain balance in remuneration and incentives, and limit strategic pricing of pharmaceuticals in reimbursement systems (*10*, *12*) – the South African case study presented later is one such example (see Section *5.2*). It should be noted that dispensing fees can add significantly to the patient price of low-cost medicines potentially putting them out of the reach of poor patients. Recent papers have compared pharmacist remuneration strategies and the use of dispensing fees across various countries and can be consulted for more detail (*Appendix 10*) (*45*, *46*).

In summary, a variety of approaches are used for regulating mark-ups from simple fixed percentages to more complex models. However, LMICs for which data is available are relatively few in number and not representative of the population from which they are drawn. As such it is not possible to draw meaningful and generalisable conclusions or make recommendations as to which approach may be the most effective or suitable for countries with limited resources and infrastructure.

4.10 Impact of mark-up regulations on medicine prices

The relatively widespread use of mark-up regulation in HICs suggests that statutory mark-ups can be effective in price regulation when used as part of a comprehensive regulatory strategy (*14*, *21*, *47*). Those countries with relatively unregulated markets in Europe tend to have higher prices (*20*). Martikainen and colleagues (*48*) found that European countries without regulation of wholesale margins tended to have higher wholesale prices (for eight new, reimbursable medicines) than in those with regulation. However, the same might not hold true for multi-source products. Reductions in mark-ups in 2005 in the UAE, where distribution margins as well as final retail prices are regulated, were reported to have the effect of reducing prices by 7% on average, with a further reduction lowering prices by around 11%, although data was not presented to support these conclusions (*49*).

In HICs regulated mark-ups and/or margins are usually strictly enforced, and therefore reducing the mark-ups can be expected to have a downward effect on final selling prices where this or the manufacturer selling price is also regulated (thus preventing additional charges being added to make up for lost revenue). The effects of price regulation in MLICs may be different due lack of information on pricing and lack of appropriate resources for analysing price information and implementing price regulation (*14*). However, the literature has very few examples of the impact of regulating mark-ups in LMICs. A few were encountered but were usually anecdotal or opinion-based rather than founded in evidence and all but one involved MICs (*Table 6*).

Table 6. **Examples of effect of mark-up regulations on medicine prices in LMIC**

Country	Pricing intervention	Impact/effect	Source
China	Distribution mark-ups enforced	Created incentive to use higher cost medicines	(*34*),(*36*)
Ecuador, Panama	Mark-up regulation	Uniform prices; reduced speculation	(*22*)
Honduras	Mark-up regulation	Higher prices; suppliers over-invoice to recover margin	(*22*)
Jordan	Remove price controls including mark-ups on 50 OTC medicines	Prices increased and controls re-imposed	(*50*)
Kenya	Price and mark-up regulations removed	Anecdotally, prices decreased	(*51*)
South Africa	0% mark-up on hospital medicines	Drop in price index of 1000 medicines	(*52*)

A report on pharmaceutical policies in the Americas stated that Ecuador and Panama were satisfied with their pricing mechanisms which utilised regulation of wholesale and retail mark-ups along with other measures (*22*). It was felt that the policies led to uniform prices and reduced speculation. Honduras, on the other hand, felt that their pricing mechanism had led to higher prices due to suppliers invoicing for more supplies than actually provided to offset the effects of regulated mark-ups.

In South Africa, the introduction of a 0% mark-up policy in private hospitals resulted in a drop in the price index for 1000 medicines monitored by the Hospital Association of South Africa (*52*). This example illustrates that changes can have an effect, at least within a defined market sector, but also stresses the importance of price monitoring to be able to assess the effects of such policy changes. Jordan, on the other hand, sought to liberalise the prices of 50 over-the-counter (OTC) medicines from price controls believing that price competition would reduce prices. However, due to other factors influencing the pharmaceutical market, the expected outcome was not achieved and the decision was reversed (*50*) suggesting that, in this case, strictly enforced mark-ups had helped to contain prices. In Kenya, there is an anecdotal account that prices in the private sector reduced after the lifting of price and mark-up regulation (*51*). If true, the reasons for this can only be speculative but could include a return to free market principles from a situation where perverse incentives or other factors had led to unnecessary high prices.

China has tried implementing medicine pricing reforms, including mark-up regulation, since the 1980s (*34*, *35*, *36*, *52*, *53*, *54*). Until 2000, mark-ups of 15% were enforced on wholesale and retail prices of medicines but this was found to be contributing to incentives to use higher cost medicines. This led the authorities to regulate a maximum retail price for selected medicines by controlling prices throughout the supply chain, including a cap on distribution mark-ups, although this policy also required revision after monitoring its impact.

Given the limited literature on this aspect, it is not possible to draw conclusions as to whether regulating mark-ups in LMICs leads to price stabilisation or reduction. However the few examples do suggest that while it is easy to think of regulation of mark-ups of having an immediate and clear impact on medicine prices, one must always consider the incentives, sometime perverse, and disincentives which are created as well as alternative mechanisms whereby the players in the distribution chain may seek to recover what they see as lost profit. For example, wholesalers may enter into agreements with importers to share the importer mark-up; additional distribution stages may be created to garner multiple mark-ups; wholesalers and retailers may charge 'administration fees' on top of mark-ups. These behaviours have been seen in practice. In Mozambique, importers have been found to collude with their suppliers to inflate landed costs as a means to circumvent pricing regulations and increase profit margins (*56*). In contrast, private hospitals in the Philippines threatened to sell medicines at regulated prices but increase other patient fees to make up for reductions in revenue following the introduction of price regulations (*57*). This can be compared to a case in China where a change in regulations to reduce medicine prices in hospitals did not lead to the expected reduced medicine expenditures. Since hospital finances depended on pharmaceutical sales, prescribers switched to using medicines off the regulated list (*34*, *58*). It was argued that the government's attempts to try and control only mark-ups in the hospital sector failed because the existing incentives and disincentives in the market on both supply and demand sides, which simply resulted in medicine switching and increased consumption, were not recognised. Other studies have shown failures in attempts to regulate/deregulate the Chinese pharmaceutical market (*34*). More comprehensive and planned strategies have had greater effect (*35*, *36*, *53*, *55*, *59*).

Similar examples have been seen in HICs such as in France where retailers were found to be purchasing generic medicines directly from manufacturers, thereby bypassing wholesalers and increasing their profit margin (*60*). There have also been recent high-profile cases of fraud in both the USA (*61*) and Canada (*38*) related to circumventing regulated prices within health insurance systems, although not directly related to regulated mark-ups. In addition, even if individual medicine prices are reduced, total pharmaceutical expenditure still often rises due to increased volume of sales and switching to higher priced products (*62*). Policy changes on price regulation - and mark-ups in particular - can have unexpected effects and cannot be predicted with certainty, which underlines the need for robust price monitoring mechanisms to be established in advance. A means of monitoring the use of medicines should also be in place since this is a more direct measure of access and can detect the wider effects of the pricing regulations.

4.11 Enforcement of mark-up regulations

Little information is available about the extent to which reported mark-up regulations are enforced but this has been identified as a potential difficulty particularly in lower-income countries which have limited resources and infrastructure (*1, 9, 15*).

In most high-income OECD countries, it is commonly assumed that price regulations are relatively strictly enforced although published evidence to support this may not be available. Information from WHO/HAI survey reports[a] indicate that Gulf countries e.g. Kuwait, UAE, and possibly other Arab countries, have strict enforcement of wholesale and retail mark-ups.

[a] http://haiweb.org/medicineprices

However, the report for Pakistan suggested that mark-ups were not completely enforced, with 3 out of 20 originator brand medicines having prices 17% – 50% higher than the regulated price (based on maximum or fixed percentage mark-ups) at significant numbers of retail pharmacies. More systematic problems were reported for other countries: official margins in Chad were found to not be respected and prices in Yemen deviated substantially from those predicted with official mark-ups. However, it is not possible to draw robust conclusions from the data since most studies did not specifically set out to examine adherence to pricing regulations.

Apart from the surveys using the WHO/HAI methodology, there are other accounts which illustrate or suggest that LMICs do face difficulties in effectively enforcing statutory mark-up regulation (*see Table 7*). Russo and McPake studied the pharmaceutical market in Mozambique where prices in the growing private sector are "regulated through a cost-plus system fixing cost and profit mark-ups for each stage of medicine distribution" (*56*). They found that the regulated mark-ups were not followed or enforced, importers and other distribution actors could negotiate with manufacturers/international suppliers to inflate landed costs so as to achieve predetermined profit margins, and retailers modified their mark-ups in line with market forces.

An investigation of pharmaceutical pricing structures and operations in Ghana found that few of the 48 public health institutions followed the Ministry of Health regulations on retail mark-ups (10% flat rate) with most charging high mark-ups on low-cost items and reduced mark-ups on high cost products (*63*). In addition, while qualitative data indicated that respondents felt that their average mark-ups was close to the regulated value, quantitative data showed it to be around 31% on average - three times the official rate.

Table 7. **Examples of enforcement of pharmaceutical mark-up regulations in LMIC**

Country	Comment	Source
Chad	Official mark-ups in the public sector not respected	*WHO/HAI*[a]
Costa Rica	Difficulties in monitoring wholesale and retail margins, and in enforcement	*(22)*
Ghana	Few of the 48 public facilities followed government regulations and knowledge of the regulations was poor	*(63)*
India	Small discrepancies between official and actual prices	*(32)*
Kosovo	Anecdotal account that regulated retail mark-up of 15% commonly flouted	*(15)*
Mozambique	Regulated mark-ups not implemented nor enforced	*(56)*
Nepal	Distribution partners were aware of regulated mark-ups but commonly applied higher mark-ups	*(64), (65)*
Pakistan	Three of 20 originator brand medicines had prices 17 – 50% higher than the regulated price at retail pharmacies	*WHO/HAI*
Russia	Ineffective enforcement of wholesale and retail mark-ups noted	*(66)*
Vietnam	Implementing regulations, needed to support decree for regulation of mark-ups, not enacted	*(67)*
Yemen	Actual prices found to deviate significantly from those predicted with official mark-ups	*WHO/HAI*

[a] WHO/HAI: http://www.haiweb.org/medicineprices

Levison (*15*) reported that the official retail mark-up in Nepal was 16% but due to a lack of official monitoring and public demand it could reach 100%. This was confirmed in the reproductive health commodity survey (*64*) in 2005 which found that the average cumulative mark-up on the 12 tracer items went as high as 80% - twice the official allowable level (26% for locally produced products and 42% for imported products); ampicillin 500mg tablets/capsules had a cumulative margin of 259%. Mark-ups varied between regions of the country and oral contraceptive products had 'cumulative margins' lower than the maximum levels set by the regulatory authority. Interviews with wholesalers and retailers have shown that while the agents are aware of the maximum 'margins' they do not necessarily apply them; bonuses may increase the margin above the maximum official level and retailers may demand a share of wholesaler profits (*65*).

More briefly, it has been reported that the 15% fixed retail and wholesale mark-ups in Kosovo were not strictly enforced and could vary between 15%-60% (*15*), while the difficulties in both enforcing regulations as well as monitoring the profit margins of wholesalers and retailers, have been cited as reasons why Costa Rica has not been able to maintain effective price controls with regulated margins (*22*). Small discrepancies between official and actual prices were noted from a survey in India (*32*), and a World Bank report has stated that one of the reasons for the high prices of medicines in Russia is "the ineffective enforcement of controls on wholesale and retail mark-ups for medicines" (*66*). Finally, Vietnam has enacted various decrees and regulations in an attempt to control the prices of medicines. One decree (Decree 120/2004/ND-CP) allowed for the setting of maximum distribution mark-ups. These were to be set by the Ministry of Finance but were never implemented, whether due to lack of political will, lack of coordination between ministries, or other factors (*67*). It is not clear whether the authorities would have been in a position to enforce the regulations if they had been implemented.

In addition to the limited country experience summarised above, there is evidence and argument from the more general medical and economic literature that enforcement of regulation in the health sector of low-income countries is more complex than might first be thought. Enforcement capabilities may be particularly weak in sub-Saharan Africa and governments in Asia have been shown to overestimate their abilities to regulate through 'command and control mechanisms' without sufficiently recognising the impact of incentives and other influencing factors (*12*, *68*, *69*).This literature, and the experiences documented in the current paper, suggests that countries that are intending to implement regulation of mark-ups should ensure they also give due thought to what is required to implement their regulations; what the impact of their intervention is intended to be, and what unintended effects may be produced. A mechanism for monitoring the effects of implementation of the regulations is imperative.

4.12 Viability of wholesalers and retailers

It is clear that regulating mark-ups can have very significant impact on the viability of commercial operations, whether these are in the public or private sector. For example, it has been estimated that cost-containment measures in European countries have reduced wholesalers' margins by more than 25% during the 1990s according to an industry-funded study (*8*). While increases in operating efficiency may be expected to allow players to stay in the market, if costs are regularly or drastically cut, a point will be reached where this will affect the viability of businesses and is likely to lead to consolidation and integration of wholesalers and/or retailers and possibly challenge the integrity of the supply chain as low-cost supplies are

sought. This may be contrary to national economic priorities and be politically difficult, particularly in LICs which often promote small businesses. It should be noted that where medicines are imported, exchange rate fluctuations can have important effects where mark-ups are fixed along with the final selling price.

In the private sector, revision of pricing regulations in general, especially where this is done with the express intention of lowering mark-ups and medicine prices, can be expected to be met with resistance from those with vested interests particularly where they feel their livelihood is threatened. Examples of this have been seen in Australia (*70*), Ireland (*71*, *72*), Mali (*72*), Russia (*74*), and South Africa (*4*, *27*), where pharmaceutical manufacturers and pharmacy trade and professional bodies opposed changes to existing regulations expressing concerns of viability. In South Africa, these concerns were substantiated by judgement of the Constitutional Court, that there was evidence that some pharmacy businesses would be threatened by proposed changes to dispensing fees (27). Regulators need to be prepared for this and must consult widely beforehand to seek consensus and avoid unnecessary confrontation.

In the public sector, if mark-ups are used to finance medicine purchases and/or other operations, any reductions in income from this source will have to be met with income from other sources or efficiency savings, else services will be affected. This effect was noted in a sample of health centres in Zaire (Democratic Republic of Congo), when doctors tried to make healthcare more affordable by lowering the cost of medicines (*75*). Medicine costs were controlled relative to inflation, but after six months of this policy, six out of eight health centres were in deficit since a significant income source had been curtailed. Further evidence of how lack of appropriate costing and economic studies can result in either inefficient operations or loss-making entities has been shown in Ghana (*63*, *76*).

From the literature search for this review, there was scant evidence of actual impact of mark-up regulation on viability of wholesalers and retailers in LMICs. Decisions on regulation need to forthrightly address this issue within the country context and in the light of health and economic policies to ensure that wholesalers and retailers receive adequate remuneration and that provision of pharmaceutical health services does not suffer. Particular attention may need to be paid to geographic access i.e. that providers supplying rural or other isolated communities are able to continue to operate. Waning and colleagues (*41*) have shown that retail pharmacy operators in Kyrgyzstan did not apply a uniform mark-up across all products, and that the costs of operations as well as income varied with distance from major population centres (*see Box 2*). The difficulty in balancing the regulation of prices with ensuring viability of commercial pharmaceutical services was observed in South Africa where a new dispensing fee for retail pharmacists was calculated based on a ‘small, efficient retail pharmacy’ (*77*). The Constitutional Court determined that this adversely affected smaller businesses, particularly those in rural areas or those operating courier or mail-order dispensing (*27*, *28*).

Observations from other countries provide further support. The prices of medicines in retail pharmacies in Laos were noted to increase with distance from the main supply centre in Lao although this finding was not always consistent (*78*). In Peru, prices of medicines tended to be slightly higher in more remote locations (*79*) which, while not statistically significant, could be important for viability. Recent studies related to the Affordable Medicine Facility for Malaria (AMFm) in Tanzania and Zambia, have shown conflicting results with private retailers in more remote areas of Tanzania tending not to increase their mark-ups on antimalarial medicines compared to those in closer urban areas that were more subject to competition (*80*). In Zambia there was variability in mark-ups across regions and between type of retailer e.g. pharmacy,

drug store, general store, private clinic (*81*). This variability suggests that each country would needs to assess how best to address geographic variability in mark-ups in its own situation if they were to be regulated.

Box 2: **Pharmacy operating costs and medicine mark-ups in Kyrgyzstan**

Medicine prices and mark-ups need to take into account the costs incurred by pharmacies and allow for reasonable profits. A cost-accounting study was conducted in a small chain of pharmacies, established by a non-governmental organization to improve access to affordable medicines among rural villages without access to pharmacy outlets.

Product variable costs contributed 70% of total costs, and across the top 50 most profitable products retail mark-ups ranged from 32% to 244% in 2007. Those with higher mark-ups tended to be those with higher sales and cross-subsidized others with lower mark-ups. However, initial mark-ups on establishing the pharmacies were found to be inadequate to support operations and had been steadily increasing from 2005 to 2007.

It was noted that the mark-ups might be considered 'excessive' (>150%) if seen in isolation, but were necessary to ensure sustainability of operations given the cost of business in the region. Profitability was related to population size of the community but also to distance from the central warehouse of the supplier. However, there was room for variations in the mark-ups in order to promote essential medicines and scope for changing mark-ups on non-health products and staff remuneration in ways which could lead to lower medicine prices.

The authors argue that a similar approach, tailored to a region or country's specific situation, could be used to determine appropriate mark-ups for private retail pharmacies and form the basis of comparison and potentially regulation of prices. Whether this could be translated easily into regulation of mark-ups is unclear given the wide variation of mark-ups that was observed, the balance of which could vary between regions/countries and the results showed that inappropriate control of prices or mark-ups would have important effects on pharmacy operations and viability.

Source: Waning et al. 2010 (41)

Determining appropriate remuneration is not easy. While there may be room for efficiency savings, larger operations and less remote operations are more likely to realise these than those serving small populations in remote and isolated areas (*13*, *41*, *78*). In addition, other health services may be cross-subsidized by charging higher mark-ups on medicines in public, non-profit, or private settings (*13*, *35*, *82*, *83*, *84*); reducing mark-ups on medicines may thus threaten more than access to medicines. Balances are needed to ensure cost-effective services are being subsidized. Furthermore, where pricing or other policies are concurrently used to promote the use of generics, current costs may not reflect those that will operate under the regulations since generic medicines generally have lower margins for wholesalers and retailers while incurring the same operating costs as the usually higher-priced originator brands. Thus access to low-cost medicines may be threatened and it could also be necessary to impose additional requirements for wholesalers and retailers to provide minimum specifications of service e.g. to carry a specific range of medicines or be able to provide/deliver any medicine within a specified time frame. However, there is no published evidence of how remuneration should be determined for LMICs although the studies in Ghana provide an example of one approach for public health services (*63*, *76*) and Dumoulin and colleagues (*84*) provide a brief overview of the costs and economics of public distribution services.

5. Country case studies

The following three country case studies are examples of how two upper-middle-income countries, and one low-income country, have addressed price regulation including the regulation of distribution mark-ups. Albania maintains a system of wholesaler and retailer mark-ups whereas South Africa has moved away from regulating mark-ups to a service fee model. Mali introduced price regulation of a selected group of essential medicines which implicitly included control of mark-ups although they were not directly controlled.

5.1 Albania

Background

Albania revised its medicine pricing policy in 2005 in the light of policy changes made in other European countries, and to address weaknesses observed in the 1994 Law on Medicines. The Reimbursement Department (DCRB/PDRD *Departamenti i Rimbursimit dhe Cmimit te Barnave*) at the Health Insurance Institute (HII), in collaboration with Pharmaceutical Directorate (*Drejtoria Farmaceutike/DF*) in the Ministry of Health and the Drugs Pricing Commission, are responsible for determining prices and reimbursement levels on an annual basis. Agents for international manufacturers and local producers are required to submit the necessary information on pricing to the Commission. Medicine prices are set based on the manufacturer's CIF (cost, insurance and freight) or ex-factory price with official mark-ups for wholesale and retail.

The ex-factory/CIF prices can be set freely and the same pricing mechanism is employed for all classes and types of medicines, whether originator brand or generic, prescription-only or OTC (over-the-counter), reimbursed or non-reimbursed. There is a white or positive list of medicines for reimbursement under the HII and the prices of more costly medicines on this list may be negotiated at the manufacturer level with external reference pricing. Internal reference pricing is used for most medicines on the positive list. The generic medicine with the lowest price within a group gets a preferred position on the reimbursement list in which patients pay a lower co-payment which stimulates competition. Wholesale and retail margins are set annually as proposed by the Drug Pricing Commission after negotiations with marketing authorisation holders or their representatives. Hospital medicines are procured by tender and supplied free of charge to patients so are not covered by this mechanism.

Mark-up regulation

Statutory mark-ups are used for remuneration of wholesale/distribution and retail operations/pharmacists. There are no other charges e.g. dispensing fees.

Regulation of mark-ups for pharmaceuticals was introduced in Albania in 1995 (15% on CIF for wholesalers; 35% on wholesale prices for pharmacies). This was amended in 1998 (12% for wholesalers; 27% for pharmacies) and in 2005 (18% wholesale; 33% retail). In the latter

amendment, certain high cost and reimbursable medicines were assigned lower mark-ups. The latest amendment in 2007 saw greater separation between reimbursed and non-reimbursed medicine through the positive list with mark-ups of 12 and 29% (reimbursed) and 18% and 33% (non-reimbursed) for wholesalers and retailers respectively.

Wholesale mark-ups

Reimbursed and non-reimbursed medicines receive different wholesale mark-ups – a fixed 18% on the manufacturer's price for the former and 12% for those which are reimbursed. The mark-up is officially divided between the importer and the wholesaler (12.5% and 5.5% respectively for non-reimbursed medicines). There are specifically named, prescription-only and usually high cost medicines which receive a special wholesale mark-up e.g. somatotropin injection (8%), insulin glargine (10%). These mark a first step towards a regressive mark-ups system to reduce the incentive to distribute higher value items.

Retail mark-ups

Retail pharmacies incur a fixed percentage mark-up on the pharmacy purchase price from wholesalers. This is 33% for non-reimbursed medicines and 29% for medicines that are reimbursed. There are again lower mark-ups for a selected list of higher-priced prescription-only medicines.

Discounts / Rebates

While not banned outright, there is no legal basis for discounts or rebates in the medicines supply chain with fixed manufacturer prices, and wholesale and retail mark-ups (and medicines provided free to in-patients).

Enforcement and effects

No evidence is available of the enforcement or effects of the mark-up regulations. However, since the mark-ups are related to reimbursement under a national health insurance, the government has a financial interest in enforcing the regulations and it is likely that they are enforced to a greater or lesser degree.

Further information

Albania country profile on the PPRI website[a].

5.2 South Africa

Background

Following independence in 1994, the South African government has sought to introduce policies to redress imbalances in the provision of healthcare within the country, including increasing access to essential medicines for the disadvantaged. A national medicines policy was developed and published in 1996 to map the strategies for achieving this. One chapter of the National Drug Policy for South Africa addressed medicine prices specifically so as to "promote

[a] http://ppri.oebig.at/Downloads/Results/Albania_PPRI_2009.pdf

the availability of safe and effective drugs at the lowest possible cost". The measures to address this were specific and built on previous commissions examining the high cost of pharmaceuticals in South Africa. They included:

- Establishment of a multidisciplinary Pricing Committee.
- Total transparency in the pricing structure of medicines.
- Use of a non-discriminatory pricing system in the private sector.
- Replacement of wholesale and retail mark-ups with a fixed professional fee.
- Establishment of a system to support free or subsidized provision of medicines in the public sector.
- Development of a price monitoring system compared to international medicine prices.
- Regulation of medicine price increases.
- Provision of priority medicines from public sector to private sector if required.
- Promotion of the use of generic medicines.

Other aspects of the policy addressed promotion of rational medicine use and the advertising and promotion of pharmaceuticals. Implementation of the policy, however, was not easy not only due to the resistance from those with vested interests, but also due to the lack of any clear blueprint or guidance for execution. Important steps and factors in the implementation of the pricing regulations were:

- **Changes to legislation**: the medicines laws and regulations needed to be changed to outlaw discounts and other perverse incentives in the supply chain, to allow parallel trade, to establish the pricing committee and 'a transparent pricing system', to permit generic substitution, and to licence dispensing doctors. These were initially challenged by the pharmaceutical lobby and were only effected in 2003.

- **Support by civil society**: The support of local and international civil society was crucial in convincing the pharmaceutical industry to withdraw its challenge of the changes to the legislation which would allow greater access to affordable medicines, and to the US government removing South Africa from the Special 301 Watch List. Linking the issue to access to antiretroviral or other essential medicines for people living with HIV/AIDS provided a focus for these efforts.

- **Consultation with stakeholders**: The South African government had to hold wide-ranging consultations in order to develop and implement the regulations, but also in determining rational and suitable prices and remuneration scales. Some of these were forced on the government by the courts after early consultations were found to be inadequate. Initial proposals to cut manufacturer prices were scaled back to essentially maintain prevailing prices and, the proposed dispensing fee has been revised following legal challenges from the pharmacy profession, going all the way up to the Constitutional Court (as of September 2010 this matter was still not resolved). However, the courts did recognise that the government had a right to intervene in matters of medicine pricing and access as allowed by the medicines act.

- **Education of consumers**: This has also been an important aspect of introduction of the price regulations, that consumers were aware of their rights, and have access to price information. This assists in enforcement in a transparent system. In South Africa, prices have to be displayed on the packaging, a database of prices is publicly available (although not in a user-friendly format[a]), and pharmacy receipts must separate the SEP (Single Exit Price) from the price paid by the consumer.

- **Consistent, high-level political support**: Throughout the various challenges raised to the changes in the legislation and the proposed pricing mechanism, the Government of South Africa showed resolve in its intent to implement the policy based on what it saw as sound and just reason.

Particular difficulties have been experienced in determining appropriate pharmacist remuneration. The move away from percentage-based mark-ups to a professional fee, as envisaged in the medicines policy, was not fully implemented – initially a capped percentage mark-up was proposed but this later changed to a combination of a percentage of the manufacturer SEP and a fixed fee (*see Box 3*). The court challenges elicited that the fee should be based on a rational process, involve transparent consultation with stakeholders and not be seen to adversely affect any sector of the market e.g. small pharmacies in rural areas, or mail-order pharmacies. International benchmarking of medicine prices has also not been effectively introduced as appropriate mechanisms for doing so are developed which are appropriate for a country in South Africa's socio-economic position.

[a] http://www.doh.gov.za/department/medic_prices-f.html

Box 3: **Dispensing fee for pharmacists – South African case study**

In 2004, the South African government undertook a radical reform of the pricing of medicines within the private health sector as part of moves to make medicines more affordable and pricing more transparent. The prices of medicines were to be regulated from the manufacturer through the entire supply chain. Revised dispensing fees formed part of the reforms. In the past, pharmacists had levied fixed percentage mark-ups which encouraged dispensing of more high priced medicines.

Initially, a single dispensing fee per item of 26% of the regulated manufacturer's selling price (single exit price) capped at a maximum R26 was proposed. This was met by strong protests and legal challenge particularly by smaller community pharmacies that saw their profits and livelihoods threatened. This ultimately resulted in a renewed consultation process following a Constitutional Court ruling.

In determining an appropriate dispensing fee under the review, it was noted, "that the viability of a retail pharmacy is influenced by both its ability to generate income and the level of its operating expenses, which in turn are each influenced by a number of factors.
Income from dispensing activities is influenced primarily by:

- Number of items dispensed
- Distribution of the value of items dispensed
- Dispensing fee

The key factors influencing expenses in the dispensary of a pharmacy include:

- Number and skills mix of professional staff
- Other recurrent expenses such as rent, electricity, insurance, etc.
- Quantity and type of capital equipment".

Taking a small efficient retail pharmacy as the basis for calculating the new dispensing fee, the 4-tier fee structure shown below was proposed (R1 ≈ USD7).

Regulated single exit price/ pharmacy purchase price (SEP)	**Dispensing fee proposal (November 2006)**
< R75	R7 + 28% of the SEP
≥ R75 and < R250	R23 + 7% of the SEP
≥ R250 and < R1,000	R26 + 5% of the SEP
≥ R1,000	R31 + 3% of the SEP

Pharmacy associations were still not satisfied with this proposal, particularly for community pharmacies serving marginal communities and, as a result of the opposition and court challenges, an amendment was proposed in June 2006. Due to continued opposition from and concerns for the viability of smaller and geographically isolated operators, an amendment in November 2009 was tabled whereby retail pharmacies could apply for an exemption from the regulated dispensing fee based on set criteria. In 2010, the government proposed a final revised mark-up structure:

Regulated single exit price/ pharmacy purchase price (SEP)	**Dispensing fee proposal (November 2010)**
< R75	R6 + 46% of the SEP
≥ R75 and < R200	R15.75 + 33% of the SEP
≥ R200 and < R700	R51 + 15% of the SEP
≥ R700	R121 + 5% of the SEP

Sources: Government of South Africa 2006 (77), 2010 (86, 87); Khan 2006 (88); Thom 2006 (89), Gray 2009 (27); Khanyile 2010 (90)

Price Regulation

The Department of Health established a Directorate of Pharmaceutical Economic Evaluations along with a pricing committee as allowed under the amended legislation. The Directorate requested pricing and operating cost information from pharmaceutical stakeholders to inform the Pricing Committee and allow determination of an initial appropriate fee structure. The Pricing Committee was comprised of experts in health economics and pharmacoeconomics, as well as representatives from the government ministries (e.g. Trade and Industry, Health), and private sector and consumer representatives (excluding the pharmaceutical industry). A maximum "single exit price" (SEP), "the only price at which manufacturers shall sell medicines" in the private sector was set based on average 2003 prices of medicines calculated on a unit basis. The SEP incorporates a logistics fee for distribution. The regulations only allowed the SEP to be increased on an annual basis to a level determined by the State and the same price must be offered to all buyers.

Wholesaler remuneration

The SEP includes a logistics fee to cover the costs of distribution of pharmaceuticals. Rather than regulate the wholesaler or distribution mark-up, it is left to the importers/manufacturers and intermediate suppliers to negotiate how the logistics fee is split. While the negotiations are not public, nor the contracts made between wholesaler or distributors and the manufacturer, the final logistics fee is. Logistics fees appear to be 10%-15%[a] and are determined by the State.

Retailer remuneration

As discussed earlier in this paper, there have been a number of difficulties in determining an appropriate structure for pharmacist remuneration. Initial proposals were for a fixed percentage mark-up (26% of the SEP) which was capped. Legal challenges by sections of the pharmacy profession have led to the current structure which incorporates regressive percentage plus a fixed fee (*see Box 3*).

Discounts/rebates

Discounts, rebates and other forms of commercial incentives are not permitted under the revised legislation. The SEP is set irrespective of the volume of sales or size of package.

Enforcement and effects

Little information is available about the enforcement or effects of the pricing regulations in South Africa apart from limited data from Pillay (*94*) although it is generally assumed that they are being enforced. A 5-year analysis of sales data has shown that sales of generic medicines (by volume) exceeded those of originator brands in 2007 for the first time (*94*). This is probably a result of policies and laws promoting generic prescribing and substitution rather than pricing regulation. While the retail professional fee debate remains to be settled, there is reportedly now no difference between medicine prices in rural and urban areas and prices of medicines have reduced by an average of 19% (25%-30% for generics and 12% for originator brands). The Pricing Committee has been the subject of attack in the media and through lobbying.

[a] http://www.doh.gov.za/docs/misc/asepi-f.html

Further information

Bond 1999 (*92*); Fisher & Rigamonti 2005 (*93*); Gray 2009 (*27*); Government of South Africa 2001 (*91*), 2006 (*77*); Hassim *et al.* 2007 (*28*); Pillay 2010 (*94*).

5.3 Mali

Background

Up until 1985, Mali imposed public control on the supply chain of pharmaceuticals. This was opened to private players in 1985 which saw the increase in private wholesale and retail activities. However, these market reforms also saw an increase in the price of medicines. An attempt to try and lower medicine prices through competition regulations in 1992 was not successful. Subsequently, in 1998, Mali adopted a national medicines policy in which was enshrined the principle of essential generic medicines, along with rational prescribing and dispensing, at least for the public sector. In line with the policy objective "to make essential medicines of quality available geographically, physically and financially to the population", a decree was passed in 2003 which sought to set the prices of medicines in public health facilities. The ultimate impact was that these medicines became unavailable in the public sector and patients, most of whom have no health insurance, were forced to purchase them in the private sector at much higher prices. In response to this, further regulations were promulgated in 2006 in which the maximum prices of 107 essential medicines were set at wholesale and retail levels in the private sector. This was done in consultation with public and private sector wholesalers, and taxes on these medicines were also reduced. In addition, various other policies have been implemented to make certain medicines free of charge in the public sector.

Public sector pharmaceutical supplies are made available through a central medical store (*Pharmacie Populaire du Mali* or PPM). The medicines are sold on to public and non-profit private health facilities. The PPM is also permitted to sell directly to private for profit retail pharmacies. There are two major private wholesalers that between them control over 80% of the market.

Mark-up regulation

Mark-ups are not officially regulated in Mali in the private sector. Rather, as part of pharmaceutical registration, manufacturers propose a retail selling price that is agreed with the Pharmacy and Medicines Department (*Departement de la Pharmacie et du Médicament*). Wholesalers then decide on what will be the wholesale selling price and this effectively determines the retailer's mark-up or margin.

Wholesale mark-ups

Wholesale margins are not officially regulated for the 107 3 essential medicines. Rather, retail prices are set in consultation with the manufacturers or importers. The wholesalers (effectively the two largest wholesalers) then determine what the wholesale selling price will be. This is determined through co-efficients applied through the following formulas:

Coefficients For Branded Products
(originator brands and branded generics)

Wholesale Price before tax (PGHT) x 1.97 = Pharmacy price
Pharmacy price x 0.75 = Wholesaler transfer price

Coefficients For Unbranded Generic Products

Wholesale Price before tax (PGHT) x 2.05 = Pharmacy price
Pharmacy price x 0.65 = Wholesaler transfer price

The margin (or possibly mark-up) of the private wholesalers has been estimated to be around 13-30% for brand name products and 19-34% for generic products.

In addition to the regular pharmaceutical supply chain, the World Bank has been implementing a project in Mali for the supply of antiretroviral (ARV) medicines (World Bank MAP Project). Under this project, a central procurement and distribution agency was selected that procured, warehoused and delivered ARVs to private sector pharmacies. The agency received a 5.46% margin to cover its operations in this regard.

Retail mark-ups

As noted above, mark-ups *per se* are not officially regulated. Retail margins are determined by the wholesalers as described above. The intention in implementation was to have no significant impact on the profit margins of retailers – by promoting the procurement of low-cost generics it was estimated that even though the selling price would be reduced, the retailers margin should be maintained.

The margin (or possibly mark-up) of the private retailers has been estimated to be around 25% for brand name products and 28%-45% for generic products. The maximum margin (or mark-up) for the price regulated medicines should be 45%.

Discounts / Rebates

Discounts, trade schemes and other commercial practices are allowed and unregulated. Wholesalers can sell to other wholesalers in which case they will offer a discount of 10%-12% off the wholesale price. Preferential or high volume retail clients may also receive discounts, free stock, free meals, or other gifts or perks.

Enforcement and effects

Due to past problems in implementation, a careful process was followed in introducing the price regulations on the 107 essential medicines. This involved:

1. Establishment of a formal committee representing all involved parties, public and private (with the exception of consumer representatives).
2. Definition of a mechanism for identifying the medicines and their current prices.
3. Fixing of maximum selling prices.
4. Informing the public of the initiative through mass media.
5. Implementation through issuing of the required decree.
6. Monitoring and evaluation including monitoring of prices at wholesale and retail level.

The process was not without delays and problems related to the vested interests of various parties but the collaborative approach combined with the monitoring follow-up appears to have led to success in the implementation of the price regulation. In one study (*33*) on a sample of 49 of the 107 essential medicines, an average reduction in price of around 25% was observed by 2009, three years after implementation.

Further information

Maïga & Diawara 2006 (*95*); Maïga *et al.* 2006 (*96*), Maïga *et al.* 2010 (*73*); Maïga & Williams-Jones, 2010 (*33*); McCabe 2009 (*97).*

6. Discussion

The discussion will summarise the findings of the literature review and attempt to provide some guidance for policy-makers considering the option of regulating mark-ups in an effort to control or lower the prices of medicines.

6.1 Overview

Evidence of the regulation of mark-ups in the distribution chain in LMICs is sparse, not systematically collected and often of poor quality where it exists. However, WHO pharmaceutical indicator survey data shows that around 60% of low-income countries report regulating wholesale or retail mark-ups in either the public or private sector. Regulation in the public sector is of a comparable level in middle-income countries, but mark-ups in the private sector are more likely to be regulated in MICs (about 80-90% of countries). This is similar to the situation in HICs. Data from medicine pricing and availability surveys using the WHO/HAI methodology suggest that fixed percentage mark-ups are most common in LMICs with regressive mark-ups only applied in some higher income economies e.g. India, Iran.

There was no evidence of mark-up regulation being used as a means to promote generic dispensing directly e.g. a higher mark-up on generic products, although Indonesia has been mentioned as applying higher mark-ups on originator brand medicines in the past. The few regressive schemes and fixed fees observed do reduce or eliminate incentives for dispensing higher value medicines and may influence dispensing of generics. Generally, mark-up regulations in LMICs tended to include all medicines within the defined public or private sector rather than a particular subset. An exception was seen in the case of Mali where a selection of generic medicines had their prices regulated in the private sector, although mark-ups were not formally controlled. There is no reliable information available about the impact of mark-up regulation alone on medicine prices in low- or middle-income countries. Enforcement of regulations is also seldom covered in the literature apart from a small number of accounts of varying degrees of lax enforcement in some LMICs. These suggest that lack of effective enforcement capacity is likely to lead to failure in the regulation of distribution mark-ups.

While mark-up regulation can undoubtedly have effects on the viability of distribution operations at the importer, wholesale or retail level, there is limited reference to this in the literature. Reported differences in the retail mark-ups of medicines in the private sector depending on distance from major urban centres, suggest that there would be need for careful determination of the operating costs for businesses across geographic regions in determining suitable mark-ups if they are to be regulated. A fixed percentage mark-up appears the most common form of remuneration of retailers in LMICs. While South Africa provides an example of how regressive schemes and/or fixed dispensing fees can be used to separate the sale function from the price of the medicine and reduce the incentive to dispense higher value pharmaceuticals, there have been difficulties implementing this and countries with lower regulatory and technical capacity could struggle to effectively implement a similar mechanism.

Apart from isolated mention of discounts and rebates, there was no evidence as to whether regulation of such commercial practices would be effective in reducing medicine prices.

In contrast, although not formally part of the literature review, there is evidence that mark-ups are commonly regulated in the countries of the European Union and other HICs that have a national health system or other reimbursement mechanism for prescribed pharmaceuticals. This is usually part of comprehensive medicine price regulation which, as a whole, has been shown to reduce pharmaceutical expenditure in the short term. However, increases in volume and switching to higher-priced medicines tend to negate this in the longer term. Retailer mark-ups appear more likely to be subject to regulation than wholesaler mark-ups in HICs, and a variety of methods are used from simple flat percentage mark-ups through regressive scales combined with fixed fees or more complex formulae. High-income countries often focus their regulation on prescription medicines or those which are reimbursed. Some countries apply a lower mark-up to reimbursed medicines which, assuming a rational selection process for reimbursed medicines, could be seen as a mechanism that promotes the use of generic and more cost-effective medicines. It is assumed that HICs have rigorous enforcement mechanisms since they are the payers and have a financial interest to enforce their regulations. There are a number of different pharmacist remuneration models specific to country situations and there is no uniform approach to the regulation of discounts, rebates, trade schemes, bonuses and other commercial incentive mechanisms.

6.2 Appropriate regulation of distribution mark-ups

Due to the scant and varied nature of the evidence base of mark-up regulation in LMICs, it is difficult to make generalisable conclusions with which to guide policy.

Analysis of the literature and theoretical principles suggests that mark-up regulation **alone** is probably not an effective strategy for the control of medicine prices. It either needs to be combined with control of the manufacturer/importer price or of the final retail selling price. Without control of either the start or end price there is too much opportunity for distribution stakeholders to manipulate the market and the prices to their advantage and to offset the effects of the mark-up regulation. This can be achieved in the public sector through efficient competitive procurement mechanisms for multisource products (effectively setting the importer/manufacturer price) whereas a greater degree of complexity is faced when regulating originator brands and prices in the private sector.

Other options should also be considered which include strengthening competitive practices in the supply chain without price regulation, policies to increase the use of low-cost generic medicines, and other forms of price regulation.

Public sector

Mark-up regulation of wholesale and retail activities can be applied in the public sector provided the appropriate resources are available (*see below*). For mark-up regulation to be effective there needs to be an efficient competitive tendering process in place for procurement of medicines, along with an efficient distribution system. Care will need to be taken in large countries where multiple distribution steps are present to ensure that each is costed appropriately and that the mark-ups applied do not result in medicines being less affordable for

patients or lead to unexpected costs to the system. It is also possible that the efficiency of existing operations can be improved so as to reduce the mark-ups required. Assessment of optimisation of transport and other operations could be useful.

Private sector

Simple mark-up regulation is likely to be difficult in the private sector where:

- There are substantial differences in the populations served by and geographical access to retail outlets e.g. those smaller communities and more remote areas are likely to have higher costs and require higher mark-ups than those in large urban areas close to the operations of major wholesalers.
- Resources for enforcement are lacking.

Selective regulation

While there is no evidence base of the selective application of distribution mark-ups in LMICs, one should consider whether the whole market sector needs to be subject to price and mark-up regulation or whether only a particular segment (e.g. regulation of generic medicines) may not be required provided competition in the market can be assured. Careful analysis will be required on the incentives that will result from such measures and the effects these might have on the use of medicines.

Choice of mark-up strategy

From the limited evidence, it is not possible to recommend any particular strategy for the regulation of mark-ups in LMICs. The choice of strategy for mark-up regulation will be dependent on a number of factors related to resources available, enforcement capability, pharmaceutical market structure, health and industrial policies and other variables. Practice from high- and middle-income countries suggests that the use of regressive mark-ups is probably beneficial in terms of balancing the financial incentives for distribution or dispensing of high priced medicine at wholesale and retail level. However, it is not clear whether lower-income countries would have the necessary infrastructure and resources to effectively implement such strategies.

Determining an appropriate mark-up

There are few papers which provide guidance on how to determine an appropriate level of mark-up, and there are clearly a variety of factors involved which make the determination of an appropriate mark-up specific to each country setting. The studies of Ghana's pharmaceutical pricing (*63,76*) provide an example of a public sector costing exercise which can feed into recommendations for suitable levels of mark-ups. However, suitable expertise (which may not be available) is required to perform such an analysis. The situation in the private sector could be even more complex to understand, where an economic analysis of business and market data must take into account various factors that would influence operating costs such as:

- Inflation
- Set-up costs
- Volume of sales
- Efficiency of operations
- Wholesale/originating price
- Distribution costs for wholesalers
- Overheads including rental and utilities
- Salaries of staff and number of required staff
- Licensure costs with municipal and regulatory authorities
- Remuneration of professional services other than dispensing
- Cross-subsidies between products or core and non-core operations
- Geographical access / special cases e.g. rural or mountainous areas
- Consumable costs e.g. packaging, labelling in dispensing prescriptions
- Fair profit

Implementing mark-up regulation

A number of resources need to be available in order to effectively implement regulation of distribution mark-ups (*see Box 4*). If a number of these are lacking, as may be the case in many LMICs, it may not be appropriate to implement such a policy although there is no clear guidance outlining the minimum requirements for implementation in a resource-challenged setting. Similarly, there is insufficient evidence to provide a framework for developing and implementing mark-up regulations although the case studies from South Africa and Mali do provide some indication of the steps that are required such as development of the policy tools, consultation of stakeholders, economic analysis and instituting a medicine price monitoring mechanism.

Box 4: **Resources required for implementing regulation of distribution mark-ups**

- Intelligence of the costs of operating the various distribution functions.
- Economic expertise for analysis of the distribution costs and to determine appropriate remuneration of stakeholders or budgetary requirement
- Medical and pharmaceutical expertise for assessing incentives/disincentives in the supply chain and effects on supply and rational use of medicines
- Statistical expertise for analysis of commercial and/or medicine price data
- Expert legal advice for drafting appropriate and sound legislation
- Structures for consultation with concerned stakeholders
- A mechanism for monitoring medicine prices and use/sales
- A mechanism for regular review of regulated prices
- Adequate resources, structures and a strategy for enforcing the regulations
- A national medicines policy document providing a basis for the action
- High level political support

6.3 Summary

This paper has provided an overview of the published evidence with regard to the regulation of mark-ups in an effort to reduce or control the prices of medicines, with a focus on low- and middle-income economies. While there is a quite extensive dataset for high-income countries, information on the implementation, effect and enforcement of mark-ups in low- and middle-income countries is sparse. Based on what has been reviewed, the following key points can be identified:

- Regulation of mark-ups as part of a comprehensive price regulation strategy probably will lead to reduced medicine prices. However, regulation of mark-ups without regulation of either the manufacturer's selling price or the retail selling price is unlikely to lead to reduced medicine prices.

- Regulation of mark-ups will probably have an effect on the viability of some operators in the pharmaceutical supply chain and may adversely impact the viability of operations in more remote areas or other health services that are cross-subsidized through higher mark-ups.

- Regulation of distribution mark-ups can have unintended impacts or consequences on the availability, sale or use of medicines. Incentives and disincentives need to be mapped and potential unexpected effects considered.

- A reliable mechanism for monitoring the prices and sales of medicines in the appropriate sector or market is essential to be able to judge the effects of pricing regulations, both intended and unintended.

- It is possible to use mark-up regulation as part of a generic medicine promotion policy, for example by providing higher remuneration for generic medicines or any other group of products, but this is not commonly practiced.

- Regulating mark-ups in the private sector is probably more complex than in the public sector. Improving efficiency of procurement and distribution in the public sector should be considered as a strategy to lower pharmaceutical costs.

- Regulating mark-ups without adequate enforcement is probably not effective and adequate enforcement in low-income countries appears challenging.

- Mark-ups that include a regressive component with or without fixed fees probably lead to better outcomes that fixed percentage mark-ups through their influence on financial incentives. However, fixed fee mark-ups can dramatically increase the price of otherwise low-cost medicines.

- While banning discounts, rebates and bonuses in the supply chain probably increases transparency in medicine pricing, there is insufficient evidence to say whether it leads to reduced prices

7. Future Research

- While mark-up regulation is aimed at reducing prices, there is a paucity of information as to whether the reduced prices lead to changes in consumption, or whether patients prefer higher-priced products by relating price to quality and/or efficacy. Examination of consumption patterns of low- and high-priced generic equivalents re-imbursed by health insurance is a possible avenue to assess this.

- Some studies have shown that high mark-ups may be required for sustainability of distribution operations or to cross-subsidize other services. Further information is needed to understand whether the high mark-ups in the supply chain in some countries are a result of profiteering or whether they reflect actual high costs in the distribution chain?

- The enforcement of mark-up regulations and price regulation in general has not been well described. This relates both to determining whether the regulations are enforced, mechanism of enforcement and the resources required for this to be successful particularly in low- and middle-income economies.

- Methods for monitoring the prices of medicines in a country are instrumental to monitoring the impact of regulatory/policy interventions. However, mechanisms have not been well-documented such as the level of sophistication required, range of products covered, analysis and interpretation of the data. This is something that needs further elucidation and guidance for policy-makers.

- More country case studies of price regulation need to be identified and described from low-income countries to provide models for comparable economies which face similar constraints in regulation and enforcement.

Glossary

Cap or ceiling	A maximum allowable value which a price or price component can take. May be referred to as a 'price cap' or 'ceiling price' when applied to the whole price.
Consignment or consignment inventory supply model	A model in which the supplier (manufacturer or wholesaler) makes goods available for sale through a client (wholesaler or retailer) but retains ownership of the goods. The client (consignee) only pays the supplier (consignor) for units which are sold during the contract period.
Degressive or digressive mark-up	See 'Regressive mark-up'
Differential fee or percentage	A fee or percentage charge which differs according to the type of product to which it is applied e.g. where reimbursed medicines attract one fee and non-reimbursed medicines attract a different fee
Discount	A price reduction granted to specified purchasers of a pharmaceutical product under specific conditions prior to sale.
Dispensing fee	A fee paid to the dispenser (usually pharmacy/pharmacist) to cover the costs of providing the service, professional services plus a reasonable profit. Normally a fixed fee that pharmacies are allowed to charge per prescribed item instead of or in addition to a percentage mark-up. The fee more accurately reflects the work involved in dispensing a prescription; a percentage mark-up makes profit dependent on the sale of expensive medicines.
Distributor	Strictly speaking, an intermediary between two players in the supply chain (manufacturer, wholesaler, retailer), collecting and distributing the goods for sale to the downstream player but not taking direct ownership of the goods thus having lower risks and inventory costs than wholesalers. However, in some contexts, wholesalers perform the distribution function and are referred to as distributors or wholesale distributors. In this report, the term wholesaler is generally used but should be taken to include distributors. In some cases, specific reference is made to distributors.
Distribution mark-ups	Distribution mark-ups include those mark-ups which apply to both wholesale and retail activities in the distribution channel or supply chain
Ex-factory price	The manufacturer's posted price. Discounts or other incentives offered by manufacturers result in an effective price that is lower than the ex-factory price. (PPRI glossary)
Fixed fee or percentage	A flat or set fee or percentage which does not vary according to the cost of item to which it is applied cf. differential fee or percentage. Also 'linear' or 'flat' fee or percentage
Full-line wholesaler	Also Fully-sorted. See 'wholesaler'.

Generic medicine (generic)	A pharmaceutical product which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the originator brand. Generics can be classified as 'branded generics' (generics with a specific trade name) and 'unbranded generics' (which use the international non-proprietary name and the name of the company).
Horizontal integration	Where companies in the same line of business engage in acquisitions and mergers e.g. wholesalers acquire other wholesalers
Importer/trader	An agent or agency which facilitates the importation of goods into a country
Manufacturer's selling price (MSP)	The price which the manufacturer sells their product at and includes all costs related to the production and sale of the product plus a profit margin. The manufacturer's selling price is usually referred to in the context of the ex-works or list price i.e. the manufacturer's posted price. Discounts or other incentives offered by manufacturers result in an effective price that is lower than the ex-factory price.
Margin	The difference between the purchase price and selling price, as a percentage of the selling price. The wholesale margin is the gross profit of wholesalers, expressed as a percentage of the wholesale price. The pharmacy margin is the gross profit of pharmacies expressed as a percentage of the pharmacy retail price. Note, in some texts, 'margin' is used synonymously with 'mark-up' which may lead to confusion. In this report, 'mark-up' is used throughout unless specific reference is intended to be made to the margin.
Mark-up	The difference between the purchase price and selling price, which may be expressed as a percentage of the purchase price to yield 'percentage mark-up'. A mark-up is added on to the total cost incurred by the producer/provider of a good or service in order to create a profit. The term 'mark-up' is often synonymous with 'gross profit', being the difference between the revenue from the commodity/service and the costs of providing the commodity/service before taking off overheads, operating expenses and tax. Thus, the wholesale mark-up is the gross profit of wholesalers and the retailer mark-up is the gross profit of pharmacies or other retailers.
Originator brand medicine (originator)	The first version of a medicine, developed and patented by an originator pharmaceutical company which has exclusive rights to marketing the product during the patent period. A originator product has a unique trade name for marketing purposes, its so-called brand name.
Over-the counter medicines	Medicines which may be dispensed without a prescription and which are in some countries available via self-service in pharmacies a/o other retail outlets (e.g. drug stores). Selected OTC products may be reimbursed for certain indications in some countries.
Rebate	A refund paid to the purchaser after the transaction has occurred. For example, pharmacies may receive a bulk refund from a wholesaler based on sales of a particular product or total purchases from that wholesaler over a particular period of time.
Retailer	A company that sells goods to consumers. In the pharmaceutical sector, 'retailer' is an umbrella term for facilities that dispense/sell medicines to out-patients e.g. community pharmacies, dispensaries, dispensing doctors, hospital pharmacies, pharmacy outlets, medicine chests, drugstores, supermarkets, etc.

Remuneration	The payment of a health care provider (individual or organisation) for the services provided. The services may be paid directly by the patient or by a third-party payer.
Regressive mark-up	A mark-up whereby the size or value of the mark-up decreases as the price of the product increases. This may be on a sliding scale or applied in differential (discrete) steps according to threshold prices. Also called degressive and digressive.
Short-line wholesaler	Also 'not fully-sorted'. *See* 'wholesaler'.
Trade scheme	A commercial practice used by a manufacturer or wholesaler to create incentives for greater sales among other downstream distribution partners, wholesale or retail. These might take the form of additional free units e.g. "buy 10, get 1 free", bundling sales of one item with those of another, volume or bulk discounts or other 'deals'
Vertical integration	Where companies expand their business into other areas which are complimentary to their existing core business e.g. wholesalers expand into manufacturing and retail
Wholesaler	An intermediary supplier or reseller that buys products from manufacturers or other suppliers in bulk and then sells on to other wholesalers and/or to retailers in smaller quantities. Most wholesalers also distribute the goods to their clients. Full-line wholesaler (fully-sorted): The activity of pharmaceutical full-line wholesaling consists of the purchase and sale, warehousing, order preparation and delivery / distribution of the full assortment of medicines (in range and depth) in a defined market (e.g. a country) Short-line wholesaler (not fully sorted): The activity of pharmaceutical short-line wholesaling consists of the delivery and distribution of a selected assortment of medicines in a defined market.

Note:

For standard glossaries of terminology, the reader is referred to glossaries of the PPRI and PHIS projects:

PPRI glossary: http://ppri.oebig.at/index.aspx?Navigation=r\4-

PHIS glossary: http://phis.goeg.at; http://phis.goeg.at/downloads/glossary/PHIS%20Glossary_UpdatedMay2010.pdf

Appendix 1. Search terms

PubMed

Policy search

(Regulation NOT gene) AND (Price OR Pricing OR Markup AND (s) OR Margin OR "Profit margin" OR "Price component") OR Pharmacies/economics[Mesh] OR "Private sector/economics"[Mesh] OR "Public sector/economics"[Mesh] OR "Drug industry/economics"[Mesh]

14.454 hits

Supply chain search

"pharmaceutical preparations/supply and distribution" [MESH] OR (Public sector [MESH] OR Private sector[MESH] OR ((Private OR Public) AND sector) OR Retail OR Wholesale OR “Supply chain” OR Distribution OR logistics)

2,230,237 hits

Pharmaceutical search

"Drugs, Generic"[Mesh] OR "Nonprescription Drugs"[Mesh] OR "Pharmaceutical Preparations"[Mesh] OR "Drugs, Essential"[Mesh] OR "Prescription Drugs"[Mesh] OR "Drug Utilization"[Mesh] OR "Self Medication"[Mesh] OR "drugs, generic" OR "prescriptions, drug" OR (pharmaceutical preparations) OR drug utilization OR pharmacoepidemiology OR pharmacoeconomic* OR drug costs OR (medicine[tw] OR medicines[tw] OR drug[tw] OR pharmaceutical[tw] OR medication[tw])

4,458,396 hits

Developing country search

((Developing OR Low-income OR middle-income) AND countries) OR (Low income OR Afghanistan OR (Lao OR Laos) OR Bangladesh OR Liberia OR Benin OR Madagascar OR Burkina Faso OR Malawi OR Burundi OR Mali OR Cambodia OR Mauritania OR Central African Republic OR Mozambique OR Chad OR Myanmar OR Comoros OR Nepal OR (Congo OR DRC) OR Niger OR Eritrea OR Rwanda OR Ethiopia OR Sierra Leone OR Gambia OR (Solomon Islands OR Solomons) OR Ghana OR Somalia OR Guinea OR Tajikistan OR Guinea-Bissau OR Tanzania OR Haiti OR Togo OR Kenya OR Uganda OR (Korea NOT South Korea) OR Zambia OR (Kyrgyz Republic OR Kyrgyzstan) OR Zimbabwe) OR (Middle income OR Lower-middle income OR Angola OR Moldova OR Armenia OR Mongolia OR Belize OR Morocco OR Bhutan OR Nicaragua OR Bolivia OR Nigeria OR Cameroon OR Pakistan OR Cape Verde OR Papua New Guinea OR China OR Paraguay OR Congo OR Philippines OR Cote d'Ivoire OR Samoa OR Djibouti OR Sao Tome and Principe OR Ecuador OR Senegal OR Egypt OR Sri Lanka OR El Salvador OR Sudan OR Georgia OR Swaziland OR Guatemala OR (Syrian Arab Republic OR Syria) OR Guyana OR Thailand OR Honduras OR (Timor-Leste OR East Timor) OR India OR Tonga OR Indonesia OR Tunisia OR Iraq OR Turkmenistan OR Jordan OR Ukraine OR Kiribati OR Uzbekistan OR Lesotho OR Vanuatu OR Maldives OR Vietnam OR Marshall Islands OR (West Bank and Gaza OR Gaza OR West Bank) OR Micronesia OR Yemen) OR (Upper-middle income OR Albania OR Libya OR Algeria OR Lithuania OR American Samoa OR Macedonia OR (Antigua OR Barbuda OR Barbados) OR Malaysia OR Argentina OR Mauritius OR Azerbaijan OR Mayotte OR Belarus OR Mexico OR (Bosnia OR Herzegovina) OR Montenegro OR Botswana OR Namibia OR Brazil OR Palau OR Bulgaria OR Panama OR Chile OR Peru OR Colombia OR Romania OR Costa Rica OR (Russian Federation OR Russia) OR Cuba OR Serbia OR Dominica OR Seychelles OR Dominican Republic OR South Africa OR Fiji OR St. Kitts and Nevis OR Gabon OR St. Lucia OR Grenada OR (St. Vincent OR Grenadines) OR Iran OR Suriname OR Jamaica OR Turkey OR Kazakhstan OR Uruguay OR Lebanon OR Venezuela)

1,891,262 hits

Econlit Descriptors

(DE="health production i120" OR DE="health government policy regulation public health i180") AND (DE="production pricing and market structure size distribution of firms l110" OR DE="economic development human resources human development income distribution migration o150")

3,610 hits

Policy search

KW=(Regulation OR Control OR Fix) AND (Price OR Pricing OR Cost OR Markup OR Margin OR Profit margin OR Price component)

16,872 hits

Pharmaceutical search

KW= medicine OR medicines OR drug OR pharmaceutical OR medication

5,267 hits

Developing country search

KW=((((Developing OR Low-income OR middle-income) AND countries) OR ((Asia OR West Indies OR Polynesia OR Micronesia OR middle east OR Afghanistan OR Armenia OR Azerbaijan OR Bahrain OR Bangladesh OR Bhutan OR Brunei OR Burma OR Cambodia OR China OR Cyprus OR Gaza OR "georgia (republic)" OR India OR Indonesia OR Iran OR Iraq OR Jordan OR Kazakhstan OR Korea OR Kuwait OR Kyrgyzstan OR Laos OR Lebanon OR Malaysia OR Mongolia OR Nepal OR Oman OR Pakistan OR Papua New Guinea OR Philippines OR Qatar OR Saudi Arabia OR Singapore OR Sri Lanka OR Syria OR Tajikistan OR Thailand OR Turkmenistan OR United Arab Emirates OR Uzbekistan OR Vietnam OR Yemen OR Israel OR Japan OR Korea OR Taiwan OR Turkey) NOT (Israel OR Japan OR Korea OR Taiwan OR Turkey)) OR (Africa OR Algeria OR Angola OR Benin OR Botswana OR Burkina Faso OR Burundi OR Cameroon OR Central African Republic OR Chad OR Congo OR Cote d'Ivoire OR Ivory Coast OR Djibouti OR Egypt OR Equatorial Guinea OR Eritrea OR Ethiopia OR Gabon OR Gambia OR Ghana OR Guinea OR Guinea-Bissau OR Kenya OR Lesotho OR Liberia OR Libya OR Madagascar OR Malawi OR Mali OR Mauritania OR Morocco OR Mozambique OR Namibia OR Niger OR Nigeria OR Rwanda OR Sao Tome OR Principe OR Senegal OR Sierra Leone OR Somalia OR South Africa OR North Africa OR Sub Saharan Africa OR Sudan OR Swaziland OR Tanzania OR Togo OR Tunisia OR Uganda OR Western Sahara OR Zambia OR Zimbabwe) OR Latin America OR Central America OR South America OR Argentina OR Belize OR Bolivia OR Brazil OR Chile OR Colombia OR Costa Rica OR Ecuador OR El Salvador OR French Guiana OR Guatemala OR Guyana OR Honduras OR Nicaragua OR Panama OR Paraguay OR Peru OR Surinam OR Uruguay OR Venezuela OR Mexico))

163,717 hits

KW=((Developing OR Low-income OR middle-income) AND countries) OR (Low income OR Afghanistan OR (Lao OR Laos) OR Bangladesh OR Liberia OR Benin OR Madagascar OR Burkina Faso OR Malawi OR Burundi OR Mali OR Cambodia OR Mauritania OR Central African Republic OR Mozambique OR Chad OR Myanmar OR Comoros OR Nepal OR (Congo OR DRC) OR Niger OR Eritrea OR Rwanda OR Ethiopia OR Sierra Leone OR Gambia OR (Solomon Islands OR Solomons) OR Ghana OR Somalia OR Guinea OR Tajikistan OR Guinea-Bissau OR Tanzania OR Haiti OR Togo OR Kenya OR Uganda OR (Korea NOT South Korea) OR Zambia OR (Kyrgyz Republic OR Kyrgyzstan) OR Zimbabwe) OR (Middle income OR Lower-middle income OR Angola OR Moldova OR Armenia OR Mongolia OR Belize OR Morocco OR Bhutan OR Nicaragua OR Bolivia OR Nigeria OR Cameroon OR Pakistan OR Cape Verde OR Papua New Guinea OR China OR Paraguay OR Congo OR Philippines OR Cote d'Ivoire OR Samoa OR Djibouti OR Sao Tome and Principe OR Ecuador OR Senegal OR Egypt OR Sri Lanka OR El Salvador OR Sudan OR Georgia OR Swaziland OR Guatemala OR (Syrian Arab Republic OR Syria) OR Guyana OR Thailand OR Honduras OR (Timor-Leste OR East Timor) OR India OR Tonga OR Indonesia OR Tunisia OR Iraq OR Turkmenistan OR Jordan OR Ukraine OR Kiribati OR Uzbekistan OR Lesotho OR Vanuatu OR Maldives OR Vietnam OR Marshall Islands OR (West Bank and Gaza OR Gaza OR West Bank) OR Micronesia OR Yemen) OR (Upper-middle income OR Albania OR Libya OR Algeria OR Lithuania OR American Samoa OR Macedonia OR (Antigua OR Barbuda OR Barbados) OR Malaysia OR Argentina OR Mauritius OR Azerbaijan OR Mayotte OR Belarus OR Mexico OR (Bosnia OR Herzegovina) OR Montenegro OR Botswana OR Namibia OR Brazil OR Palau OR Bulgaria OR Panama OR Chile OR Peru OR Colombia OR Romania OR Costa Rica OR (Russian Federation OR Russia) OR Cuba OR Serbia OR Dominica OR Seychelles OR Dominican Republic OR South Africa OR Fiji OR St. Kitts and Nevis OR Gabon OR St. Lucia OR Grenada OR (St. Vincent OR Grenadines) OR Iran OR Suriname OR Jamaica OR Turkey OR Kazakhstan OR Uruguay OR Lebanon OR Venezuela)

163,867 hits

Appendix 2. Distribution mark-ups applied to pharmaceuticals in OECD countries[a]

	Wholesale mark-up	Pharmacy mark-up	Fixed pharmacy fee, dispensing fee or prescription fee	VAT
Australia	7.52% of ex-factory price for the majority of PBS listed items, capped at USD 69.94.	Regressive mark-up scheme, ranging from 10% to 4%, capped at USD 40.00	AUD 5.44	No VAT (or GST) for prescribed medicines. For most OTC, 10%, unless they fall under the GST-exemption (standard rate 10%).
Austria	Two regressive mark-up schemes, depending on the reimbursement category, capped at EUR 23.74.	Two regressive mark-up, ranging from 37% to 3.9%. Pharmacy mark-ups for reimbursed medicine are significantly lower than for non-reimbursed medicines.	15% for private customers. Not under the sickness-fund scheme.	20% (standard rate 20%).
Belgium	Fixed mark-up: 13.1% of ex-factory price, with a maximum of EUR 2.18.	Fixed mark-up: 31% of the wholesale price, with a maximum of EUR 7.44.	–	6% (standard rate 21%).
Canada	Capped, but depends on region and plan. Overall average 5%.	Depending on region and drug plans	Depending on region and drug plans.	0% on reimbursed medicines (standard rate 7%).
Czech Republic	On average 5-7%. Total margin of 29% is shared with the pharmacists.[†]	On average 22-24%. Total margin of 29% is shared with the pharmacists.	–	5% levied at wholesale level (standard rate 19%).
Denmark	Unregulated. On average 4%.	New scheme since 8 April 2007: 8.8% of pharmaceutical purchase price + a constant amount.	DKK 9.25 (EUR 1.24) incl. VAT. On all prescribed medicine.	25% (standard rate 25%).
Finland	Unregulated but indirectly controlled through reimbursement system. Average margin estimated at about 2-4%.	Regressive mark-up scheme based on pharmacy purchase price (a × PPP + b).	Dispensing fee of EUR 0.42 per prescription item.	8% (standard rate 22%).
France	Regulated only for reimbursable medicines. Regressive mark-up, ranging from 10.3% to 2% of ex-factory price.	Regulated only for reimbursable medicines. Regressive mark-up, ranging from 26.1% to 6% of ex-factory price.	Flat fee of EUR 0.53 per box only for reimbursable medicine.	2.1% for reimbursable and 5.5% for non-reimbursable medicines (standard rate 19.6%).

[a] OECD *Pharmaceutical Pricing Policies in a Global Market*, 2008 (*7*)

Germany	Maximum mark-up, defined through regressive schemes combining percentages and fixed amounts: • for POM: markup ranging from 15% to 6% of ex-factory price, capped at EUR 72; • for reimbursable OTC: ranging from 21% to 3% of ex-factory price, capped at EUR 61.63.	Fixed mark-up for POM: 3% of wholesale price. Regressive mark-up combining percentages and fixed amounts for reimbursable OTC, ranging from 68% to 8.26% of wholesale price, with a maximum of EUR 118.24.	For POM: EUR 8.10.	16%, increased to 19% per 1 January 2007 (standard rate 16%).
Greece	Fixed mark-up: 8.43% of ex-factory price for all pharmaceuticals.	Fixed mark-up: 35% of wholesale price for all pharmaceuticals.	–	9% (standard rate 18%).
Hungary	All pharmaceuticals: maximum mark-up defined through a regressive scheme combining percentages and fixed amounts, ranging from 12% to 5% of ex-factory price.	All pharmaceuticals: Regressive mark-up combining fixed amounts and percentages, ranging from 26% to 17% of pharmacy purchase price, with a maximum of HUF 850 (EUR 3.43).	–	15% for pharmaceuticals (standard rate 25%).
Iceland	Fixed Margin for POM, no regulation for OTC	Fixed Margin for POM, no regulation for OTC.		14% (standard rate 24.5%)
Ireland	Fixed mark-up: 15% of ex-factory price.	Mark-up on ingredient cost, depending on patient's coverage status: • 0% for GMS patients • 50% for patients covered by Drugs Payment Scheme (DP) and Long Term Illness (LTI) scheme.	Depending on patients' coverage status: • GMS patients: Fixed dispensing fee of EUR 3.26; • Flat dispensing fee of EUR 2.86 for patients covered by DPS and LTI schemes.	0% for oral medicines and 21% for non-oral medicines (standard rate 21%).
Italy	Reimbursable: fixed margin: 6.65% of pharmacy retail price. Non-reimbursable: free margin, around 8%.	Reimbursable: 26.7% of pharmacy retail price, but regressive due to official discount to the NHS up to 5%. Non-reimbursable: free margin.		10% (standard rate 20%).
Japan	Unregulated	Unregulated	Dispensing fee and prescription fee vary with number and class of drug, dispensers, etc.	5% levied at the wholesale level (standard rate 5%)
Korea	Not fixed Average margin of 8.1% for POM (range 3.2-4.0%) Average margin of 9.5% for OTC (range 2.0-3.0%)	Formally no mark-up for POM, although implicit margins exist There is a variable mark-up for OTC	Fixed management and administration fees totaling (KRW 1 252) Dispensing fees paid according to a fee schedule with a fixed and variable component, depending on the length in days of the prescription.	10% (standard rate 10%)

Luxembourg	15.21% for products originating from Belgium or Luxembourg	50.2%; 46.7% if originated in Belgium or Luxembourg.		3% (standard rate 15%).
Mexico	Not fixed.	Not fixed.		No VAT for all medicines (standard rate 15%).
Netherlands	Not fixed.	There is a clawback of 6.82% on pharmacy prices for medicines covered by the Medicines Pricing Act (with a ceiling of EUR 6.80 per prescription).	EUR 6.10.	6% for all medicine (standard rate 19%).
New Zealand	10%.	All pharmaceuticals: 4% if price less than NZD 150. 5% if price more than NZD 150.	NZD 5.16 for most pharmaceuticals (differs for some groups of pharmaceuticals)	12.5% (standard rate 12.5%).
Norway	Unregulated. Average margin of 5-7% for patented medicine. Much higher for other drugs.	Maximum mark-ups for reimbursed and non-reimbursed medicines. 8% of Pharmacy purchase price when PPP ≤ EUR 25, and 5% for PPP > EUR 25.	NOK 21.50 (EUR 2.70).	Standard VAT of 25% (standard rate 5%).
Poland	Maximum mark-up for reimbursed medicines: 9.78% of ex-factory price (incl. VAT). No regulation for non-reimbursed drugs: average mark up: 12-14%.	For reimbursed medicines: maximum mark-up defined through regressive scheme combining fixed amounts and percentages, ranging from 40% to 12% of wholesale price, capped at PLN 12. No regulation non-reimbursed medicine: average 25%.		7% on manufacturer's price (standard rate 22%).
Portugal	Reimbursed medicines: 6.87% of pharmacy retail price without VAT. Non-reimbursed: 8% of pharmacy retail price without VAT.	Reimbursed medicines: 18.27% of pharmacy retail price without VAT. Non-reimbursed: 20% of pharmacy retail price without VAT.	–	5% (standard rate 19%).
Slovak Republic	Maximum mark-up depending on the type of pharmaceuticals: 11% of ex-factory price for reimbursed medicines and for non-reimbursed POM, 4% for very expensive drugs, 5% for OTC drugs and vaccines, 10% for "hospital only" drugs sold by pharmacies.	Maximum mark-up depending on the type of pharmaceuticals: 21% of pharmacy purchase price for reimbursed and for non-reimbursed POM, 10% for very expensive drugs (> 250), 15% for OTC drugs, 7% for vaccines and 10% for "hospital only" drugs sold by pharmacies.	Prescription fee of SKK 5 per prescription of which 25% is for the pharmacy (and 75% for the insurance company).	10% (since 1 January 2007), standard VAT 19% (standard rate 19%).

Spain	All Pharmaceuticals: 7.6% margin for drugs costing < EUR 89.62 and a fixed fee of EUR 7.37 for drugs exceeding EUR 89.62.	27.9% for generic drugs costing < EUR 89.62 and a fixed fee of EUR 37.53 for drugs exceeding EUR 89.62.	–	4% (standard rate 16%).
Sweden	Unregulated. Mark-ups negotiated between Apotek (distribution monopoly) and manufacturers. Average margin estimated 2.7%.	For POM: degressive linear mark-up capped combining proportional and fixed mark-up, capped at SEK 167 (EUR 18). For OTC, mark-ups set by Apoteket.	–	0% for POM, 25% for OTC (standard rate 25%).
Switzerland	Total distribution mark-ups are defined for reimbursed medicines and must be shared between wholesalers and pharmacists. Mark-ups are defined through a regressive linear scheme combining proportional (ranging from 15% to 8% of ex-factory price) and fixed mark-ups, capped at CHF 240. OTC: shared distribution margin.		Pharmacists' services paid according to a fee-schedule.	2.4% (standard rate 7.6%).
Turkey	For all pharmaceuticals, Regressive mark-up, ranging from 9% to 2% of ex-manufacturer's prices.	Regressive mark-ups, ranging from 25 to 10% of pharmacy purchase price.	–	8% for both POM and OTC (standard rate 18%).
United Kingdom	The NHS list price includes wholesalers' distribution margin. Discounts may be negotiated between manufacturers and wholesalers and between wholesalers and pharmacists.	Pharmacies' margins are determined by the difference between NHS reimbursement price and the actual pharmacy purchase price.	Pharmacists receive fees and allowances for their services.	17.5% POM and OTC – but practically 0% as POM is paid for by the government (standard rate 17.5%).
United States	Unregulated. Average of 2-4%.	Unregulated, average of 22-25%.	–	

Appendix 3. Potential strategies in regulating distribution mark-ups

Strategy	Description of charge added to cost price
Fixed or flat fee	A fixed amount is added to all items. No examples of this used alone.
Differential fixed or regressive fee	Items in one category incur a higher/lower fixed amount e.g. EML vs. non-EML, Prescription-only medicine (POM) vs. OTC, cold chain vs. normal. No examples of this used alone.
Regressive flat fee	Higher cost items incur a lower fixed amount. No examples.
Fixed percentage	A fixed percentage of the cost price is incurred e.g. Albania wholesale 12% on reimbursable medicines.
Differential fixed or regressive percentage	Items in one category incur a higher/lower fixed percentage e.g. EML vs. non-EML, POM vs. OTC, cold chain vs. normal e.g. Albania wholesale mark-up 12% reimbursable, 18% non-reimbursable; Latvia has separate regressive percentages for reimbursables and non-reimbursables.
Regressive percentage (whole procurement price)	Higher cost items incur lower percentages according to defined cost thresholds e.g. Turkey wholesale mark-ups are regressive 2-9%.
Regressive percentage (part of procurement price; "sequential")	Higher cost items incur lower percentages according to defined cost thresholds, with the mark-ups applied 'sequentially' to the amount of purchase price remaining e.g. Syria retail mark-ups.
Fixed maximum fee	Maximum fixed amount is regulated but lower amounts can be incurred. No examples.
Fixed maximum percentage	Maximum percentage of cost price is regulated but lower mark-ups can be incurred e.g. Poland wholesale fixed max 9.8%.
Regressive maximum percentage or fee	Higher cost items incur lower fixed amounts or percentages according to defined cost thresholds, with each specifying a maximum mark-up. e.g. Norway with maximum retail mark-ups of regressive 5-8%.

Combinations and variations	
Fixed fee + fixed percentage	No examples.
Regressive fixed fee + fixed percentage	No examples.
Fixed fee + regressive percentage	e.g. Estonia retail regressive 0-40% plus fixed fee (which is not applied to all levels and is higher for most expensive medicines).
Progressive fixed fee + regressive percentage	e.g. Sweden (note both fixed fee and percentage incurred).
Low mark-up + fixed fee	e.g. Germany retail 3% + € 8.10 per pack.
High mark-up + fixed fee	e.g. Finland retail regressive 12.5-50%+fixed fee plus € 0.42 (formula).
Fixed combined wholesale + retail mark-up to be divided up following negotiation	No examples; Switzerland? (cases where manufacturers and wholesalers negotiate on mark-ups in unregulated environments).
Regressive percentages capped with (progressive) fixed fees	e.g. Austria retail, Germany wholesale, Hungary – incur either regressive percentage or a fixed fee which acts as a sequential cap to the prior percentage threshold. The fixed fees are used "to avoid strategic pricing of drugs" (PPRI Germany).
Fixed percentage capped with a fixed fee	e.g. Spain wholesale up to € 91 7.6%; above € 91 fixed fee is € 7.54
Variations in number of categories for regressive mark-ups and their values	e.g. Wholesale Slovak Rep. has two (4%; 11%); Estonia five (3%, 5%, 10%, 15%, 20%) e.g. Germany wholesale top threshold is € 1200; Hungary wholesale top threshold is € 10.48
Other combinations/options	Belgium – fixed percentage with cap on first threshold, same percentage applied to first € 24 of next thresholds plus small progressive percentage without caps. Pricing formulas or other means e.g. Finland has a pharmacy tax or fee based on annual turnover which is included in determining the allowed retail mark-up

Appendix 4. Summary of data on wholesale and retail mark-ups in low- and middle-income countries identified in the literature

Note:mark-ups are unregulated or of unknown status unless otherwise stated; other price regulations may be in force

Country	Income category	Public wholesale mark-up	Public retail mark-up	Private wholesale mark-up	Private retail mark-up	Dispensing fee	Date of survey/ info	Source and comments
Argentina	UMIC	-	-	60%	25%	-	1995	Sarmiento (1995)(*22*)
Armenia	L-MIC	25%	25%	25-30%	25-30%	-	2002	Key informant; Levison (2003)(*15*) and WHO pharmaceutical profile 2010
Bolivia	L-MIC	-	-	30-35%	-	-	1994	Sarmiento (1995)(*22*)
Bolivia	L-MIC	184.8-488.3%	40.7-123.0%	144.0-228.1%	92.4-139.3%	-	2008	Price survey report
Brazil, Rio de Janeiro State	UMIC	-	-	See retail	27.1 – 28.8% combined wholesale and retail	-	2001	27.1 – 28.8% wholesale and retail mark-ups combined in private sector; Price survey report
Brazil	UMIC	-	-	7%	22%	-	2000	"Monitored freedom" in medicine pricing; Cohen (2000)(*98*); Levison (2003) (*15*)
Burkina Faso	LIC	-	-	30%	100%	-	2007	Antimalarials; Document review and semi-structured interviews; Patouillard *et al.* (2010)(*99*)
Burkina Faso, Cameroon, Kenya, Uganda	LIC	-	-	13% average	35% average	-	2007	AMFm technical proposal (2007)(*100*); average mark-ups across countries for ACTs
Cambodia	LIC	-	-	2-50%	3% (ACT)	-	2003	ACTs; interviews. Patouillard *et al.* (2010) (*99*)
Cambodia	LIC	-	-	-	16-71% (ACT)	-	2007	ACTs in pharmacies and drug shops; interviews. Patouillard *et al.*(2010)(*99*)

Cameroon	L-MIC	-	-	14% (ACT)	34% (ACT)	-	2007	ACTs; interviews. Patouillard *et al.* (2010)(*99*)
Chad	LIC	~44% (importer +distributor)	~44%	~22%	~38%	n	2004	Estimates based on graphic in Price survey report
Chad	LIC	-	-	20%	30%	n	2004	Generic amitriptyline and Originator Brand ciprofloxacin; Price survey report
Chad	LIC	16% (CMS importer) + 25% (regional medical store) (regulated)	30% (regulated)	20% (unregulated)	30% (unregulated)	n	2004	Official mark-ups not respected in public sector; Price survey report
China, Shandong Province	L-MIC	To hospitals: 0.6-10.3% LPG; 6.2-13.7% OB	14.1-26.1% LPG, 17.1-18.8% OB	3% gen, 2-3% OB	17.8-25.7% gen; 4.5-22.3% OB	n	2004	Losartan new on the market Price survey report
China	L-MIC	-	-	15%	15%	-	up to 2000	Reports on pricing policy; Meng *et al.* (2005)(*34*); Sun *et al.* (2008)(*35*); Yu *et al.* (2010)(*36*)
China, Hubei Province	L-MIC	-	median 44.8% (range 15.6-177.8%)	-	-	-	2007	Observed prices of 25 medicines in public hospitals; Yang *et al.* (2010)(*101*)
China	L-MIC	-	250-1000% (unregulated)	-	-	-	2005	Hospital data - source uncertain; Liang *et al.* (2009)(*44*)
Costa Rica	UMIC	-	-	30% (25% essential meds) (regulated)	30% (25% essential meds) (regulated)	-	1994	Sarmiento (1995)(*22*)
Dominican Rep.	UMIC	-	-	33-40%	30%	-	1994	Sarmiento (1995)(*22*)
Ecuador	L-MIC	-	-	20% (regulated)	25% (regulated)	-	1994	Sarmiento (1995)(*22*)
Ecuador	L-MIC	50-56% LPG	30-60% LPG	35-67.5% gen	38-54% gen	-	2008	Price survey report

El Salvador	L-MIC	-	-	380% gen ceftriaxone, 179% gen clotrimazole cream; 1,702% gen ciprofloxacin; 380% gen ceftriaxone (from India); 75% gen ranitidine; 74% gen fluconazole	552% gen ceftriaxone, 367% gen clotrimazole cream; 226% gen ciprofloxacin; 413% gen ceftriaxone (from India); 1,228% gen ranitidine; 30% gen fluconazole	n	2006	Second set of values calculated from data in text and amended based on HAI database and survey report
Ethiopia	LIC	27 - 30% gen	25% gen	20% OB; 39% gen	30%	n	2004	Price survey report
Ethiopia	LIC	-	25%	-	-	n	2002	"Special Pharmacies" operating as RDFs. Russell & Abdella (2002)(*102*)
Ethiopia	LIC	-	20-30% (official?)	-	-	n	2007	'Special Pharmacies" operating as RDFs. Carasso *et al.* (2009)(*103*)
Ghana	LIC	10% (regulated)	20% (regulated)	30-40% (unregulated)	30-40% (unregulated)	n	2004	Interviews Price survey report
Ghana	LIC	20% (imported), 15% (local);+ 10% for regional medical stores (regulated)	10% (regulated)	-	10-100% (unregulated)	-	2002; 2003	Data shows regulated public sector mark-ups not known nor enforced. Huff-Rousselle & Azeez (2002) (*76*); Sarley *et al.* (2003) (*63*).
Ghana	LIC	-	-	10-30%	30-200%	n	2009	Interviews. McCabe *et al.* (2009)(*97*)
Grenada	UMIC	-	-	20%	40%	-	2002	Snell (2003)(*51*)
Honduras	L-MIC	-	-	operating costs+4% (regulated)	27% (regulated)	-	1994	Sarmiento (1995)(*22*)
India, Haryana	L-MIC	-	-	8%	16%	n	2004	Hypothetical cases Price survey report
India, Karnataka	L-MIC	-	-	8-10% OB; 8.7-10% gen	15.3-19.5% OB; 17.9-22.5% gen	n	2004	Hypothetical cases Price survey report
India, Maharashtra (4 regions)	L-MIC	-	-	9.5-9.7% gen; 9.5% OB	19.1-20.3% gen, 19.2-20.1% OB	n	2005	Price survey report
India, Rajasthan	L-MIC	-	-	10%	20%	n	2003	In general mark-ups based on interviews; mark-ups vary and lower for originator brands

								Price survey report
India, West Bengal	L-MIC	-	-	8% scheduled; 10% unscheduled (not regulated but by agreement)	16% for scheduled (but 15-15%; higher for slow movers - interviews);	n	2004	Price survey report
India	L-MIC	-	-	2-5% for super-stockist; 8% min. scheduled medicines (regulated) – 7-11.1% actually measured; 10% non-scheduled (unregulated ave) – 9.7-11.5% actually measured (includes effect of trade schemes) (regulated)	16% min. scheduled medicines (regulated) – 17-30% for OB & 92-436% for LPG actually measured; 20% non-scheduled (unregulated ave) – 21.5-32.7% actually measured (includes effect of trade schemes) (regulated)	n	2007†	Minimum mark-ups; trade scheme increase effective mark-up. Kotwani & Levison (2007)(*32*)
India	L-MIC	-	-	-	Retail margin estimated 25%; mark-ups of 150-200%	n	2007	No evidence to support; study only examined retail prices in various sectors. Godwin & Varatharajan (2007) (*104*).
Indonesia	L-MIC	-	-	6-15%	20-35%	y (Rps100-500)	2004	Prices of some EML medicines regulated Price survey report
Iran	UMIC	-	15% (regulated)	8-13.5% (lower for imported OB but 10-13% importer mark-up) (regulated)	10-21% (lower for imported OB) (regulated)	y (5,000)	2008	Public gets medicines through private wholesalers Price survey
Jordan	L-MIC	-	-	19% (regulated)	26% (regulated)	n	2004	Price survey report
Kazakhstan	UMIC	-	-	5-50% gen (15% measured)	20-30% gen (measured)	n	2004	Price survey report
Kenya	LIC	-	-	15% (regulated)	20% (regulated)	n	2000	Fixed max mark-ups. Myhr (2000)(*105*); Reported as public sector mark-ups in Levison (2003)(*15*)
Kenya	LIC	0-15%	-	15-30%	20-100%	n	2001	Price survey report
Kenya	LIC	-	-	25%	33%	-	2001/02	Prices have dropped since regulations lifted; Snell (2003)(51)

				(regulated)	(regulated)			
Kenya	LIC	-	-	Regressive 10-22% (includes wholesale and retail?); 2% for ARVs	5% for ARVs	n	2003	Case study from faith-based supplier. (WHO 2004)(*106*)
Kenya	LIC	-	-	-	13-189%	-	2003	Antimalarials; interviews. Patouillard *et al.* (2010)(*99*)
Kenya	LIC	-	-	15% measured (importer 30-40% fee) (15-34% hypothetical)	33% OB imported; 203% gen local (33-308% hypothetical)	n	2004	15% and 33% voluntary agreement applied to OBs and high cost items Price survey report
Kenya	LIC	-	-	15%	33% OB; 203% gen	-	2004	Antimalarials; interviews. Patouillard *et al.* (2010) (*99*) (Duplication of price survey?)
Kenya	LIC	-	-	10%	33%	-	2007	Antimalarials; interviews. Patouillard *et al.* (2010)(*99*)
Kenya	LIC	0%	-	(54-748% importer); 30% OB; 6% LPG	37% OB; 102% gen	n	2007†	Price survey report
Kenya	LIC	-	-	(15-200% importer); 3-23%, ave. 14%; see also retail	Ave. 28% retail; 5-22% mark-up in mission sector	n	2008*	Interviews; Levison & Kimatu (2008) (107)
Kenya	LIC	-	-	-	38-113% (SP/AQ)	n	2002	Observed data on two most widely stocked products; Amin & Snow (2005)(*108*)
Kosovo	L-MIC	15% (see notes) (regulated)	15% (see notes) (regulated)	-	-	-	2002	Regulated mark-ups not observed. Not certain whether public or private sector. Levison (2003)(*15*)
Kuwait	HIC	-	-	35% (regulated)	26% (regulated)	n	2004	In 2005 changed to 29% and 20% Price survey report
Kyrgyzstan	LIC	-	-	15-25% OB; 25-35% gen	5-15% OB; 15-25% gen	n	2005	Price survey report
Kyrgyzstan	LIC	-	-	-	32-244%	n	2007	Data from NGO chain of pharmacies; Waning *et al.* (2010)(*41)*
Lebanon	UMIC	-	-	10% (regulated)	30% (regulated)	n	2004	Regressive mark-ups have since been introduced; Price survey report; Anon (2008)(*109*)
Lithuania	UMIC	See comments	-	-	-	-	2002	Formula with regressive percentage

								and fixed fee; Snell (2003)(*51*)
Malaysia	UMIC	17.5 – 20% (LPG and OB)	0%	5.8% gen; 15% importer+ 3.1 - 19.1% OB; (0% for locally made gen)	100% gen; 25.4 - 38.3% OB; 140% for locally made gen	n	2004	Also dispensing doctors mark-up 5-75^ for OB, 316% LPG. Importer 12%; distributor 0 -15%; retailer 50 - 317%. Price survey report and Babar *et al.* (2007)(*110*).
Malawi	LIC	-	-	10-30% (10-25% gen; 30-35% OB)	50-100%	n	2009	Interviews. McCabe *et al.* (2009) (*97*).
Mali	LIC	-	-	13.3-29.3% OB; 19.3-33.7% generics	25% OB; 28-45% generics	n	2004	Maiga & Diawara (2006)(*95*)
Mali	LIC	20-50% measured (regulated)	24-45% measured (regulated)	15% in theory at one wholesaler (23-30% measured)	100% (indicative price of one wholesaler) (45-78% measured)	n	2004	Theoretical vs. measured; Bamako public sector prices lower since no need for second wholesaler; might be cumulative values; public prices are regulated but not observed. Price survey report
Mali	LIC	-	-	-	45% max on listed medicines (price regulated; not mark-up)	n	2009	Prices of 107 essential medicines fixed and wholesale and retail margins determined by negotiation. Maiga & William-Jones (2010)(*33*).
Mali	LIC	-	-	19-34% gen; 13-30% OB (some prices regulated; not mark-up)	28-45% gen; 25% OB (some prices regulated; not mark-up)	n	2009	Interviews; Not clear whether these are margins or mark-ups; McCabe *et al.* (2009)(*97*)
Mauritius	UMIC	14%	27%	-	-	-	2002	Levison (2003)(*15*)
Mongolia	L-MIC	15%	0%	25% gen and OB	30% gen; 10% OB	n	2004	Price survey report
Morocco	L-MIC	-	-	10% gen & OB (regulated)	30% gen & OB (regulated)	n	2004	Price survey report
Mozambique	LIC	-	-	13.5% importer+9% warhousing+5% distribution (all on CIF price) (regulated)	76.3% on CIF price (regulated)	n	2007	Regulated mark-ups not enforced; Russo & McPake (2009)(*56*)
Nepal	LIC	- (see notes)	- (see notes)	10-12%	16% (regulated)	-	2002	Reported as for public sector but likely to the private sector. Levison (2003)(*15)*

Nepal	LIC	-	0% encouraged (unregulated)	7% importer+8.5% wholesaler (regulated)	16% (regulated)	n	2005	Maximum prices and mark-ups not enforced. Rao & Thapa (2005)(*64*); Harper *et al.* (2007)(*65*).
Nicaragua	L-MIC	-	-	35-67% generic; 30-128% OB	38-54% generic; 32-73% OB	-	2008	Price survey report
Niger	LIC	-	-	47.3% (importer)+35% (wholesaler)	35%	n	2009	Abdou Sidikou *et al.* (2009)(*111*)
Nigeria	L-MIC	-	-	20% importer+10%	30% (one example)	n	2004	Price survey report
Nigeria	L-MIC	-	5% profit margin from RDF	-	-	-	2005	University teaching hospital RDF; statement without supporting data; Mokuolu *et al.* (2007)(*112*)
Oman	HIC	-	-	20.9% (regulated)	28.1% (regulated)	n	2007*	Price survey report
Pakistan	L-MIC	-	-	6% imported; 2% local (regulated)	15% local and imported (regulated)	n	2004	821 controlled products; enforcement not rigorous Price survey report
Panama	UMIC	-	-	30% "ethical", 25% other (regulated)	33% "ethical"; 30% other (regulated)	-	1994	Sarmiento (1995)(*22*)
Peru	UMIC	20% importer (unregulated)	25% (regulated)	25-40% importer+ 20% (gen) to 25% (OB) (unregulated)	11% (OB) – 70% (gen) (unregulated)	n	2005	Lower retail mark-ups for OB; importer gives public procurement less mark-up due to volume; interviews Price survey report Mark-ups higher on lower cost medicines; Madden *et al.* (2010)(*26*)
Philippines	L-MIC	-	-	17.5 – 65%	20 – 50%	n	2005	Interviews Price survey report
Philippines	L-MIC	-	30% max (regulated)	18.2 – 117% (LPG); 5 – 13% (OB; theoretical) (unregulated)	2.2 - 60% (OB); 5.1 – 355% (LPG) (unregulated)	n	2008†	Price survey report with new methodology
Russia	UMIC	-	-	25% max (regulated)	30% max for essential medicines; higher for others (regulated)	-	2009	World Bank (2009)(*66*)

Russia	UMIC	-	-	15% (regulated)	25-35% (regulated)	-	2000	Bulgakov (2000)(*74)*
Senegal	L-MIC	-	-	15-18% quinine	30-41% quinine	-	2003	Interviews; Patouillard *et al.* (2010)(*99)*
Senegal	L-MIC	15%	36%	19%	50%	n	2005	May be cumulative values Price survey report
Senegal	L-MIC	-	-	15% ACTs	3-22% ACTs	-	2007	ACTs; interviews and mystery shopper. Patouillard *et al.* (2010)(*99)*
Senegal	L-MIC	20% (regulated)	50% (regulated)	14.3% (OB/specialty medicine); 6.2% (social list); 18.2% (hospital pack) (regulated)	40.7% (OB/specialty medicine); 9.9% (social list); 56.3% (hospital pack) (regulated)	n	2000	Theoretical; Guimier *et al.* (2005)(*113)*
Sierra Leone	LIC	-	-	33% own products; 25% 3rd party items	-	-	pre2002	Snell (2003)(*51)*
South Africa	UMIC	-	-	21.2%	50%	-	2003	Discounts affect final price. Gray & Matsebula (2000)(*52).* Reported as public sector in Levison (2003)(*15)*.
South Africa, Gauteng Province	UMIC	-	-	Regulated fixed logistics fee (equiv. to approx. 2-20% of MSP OB; 15% for gen) (regulated)	Fixed fee (regressive bands)	y	2004	Dispensing doctors have lower dispensing fee Price survey report
South Africa	UMIC	-	-	-	46%+ZAR6 33%+ZAR15.75 15%+ZAR51 5%+ZAR121 (regulated)	y (captured in retail mark-up)	2010	Govt of South Africa (2010)(*86)*
Sri Lanka	L-MIC	7%	12.5%	25% importer + 8%	16%	n	2001	Hypothetical Price survey report
Sri Lanka	L-MIC	- (see notes)	- (see notes)	8.5%	16.25%	-	2002	Reported as public sector but likely to be private sector; Levison (2003) (*15)*
Sri Lanka	L-MIC	-	-	(see retail)	172% (includes taxes, import, wholesale, retail)	-	2000	Weerasuriya (2000)(*114)*

Sudan	L-MIC	20%+28%(regional store) (regulated)	20%(non-RDF) (regulated)	15% (regulated)	20% (regulated)	n	2005*	Price survey – HAI database
Sudan	L-MIC	64% (all mark-ups including retail for Khartoum RDF)	See wholesale	-	-	n	2006	E-Drug message Mohammed (2006)(*115*)
Syria	L-MIC	-	-	8% (regulated)	8-30% regressive, differential /cumulative 30% SP1-40; 20% SP41-80; 15% SP81-200; 10% SP201-500; 8% or more 501 (regulated)	n	2003	Price survey report
Tajikistan	LIC	-	-	15%	15-30%	n	2005	Price survey report
Tanzania	LIC	0%	50%	-	-	-	2000	Reported as public sector but source classified other data incorrectly; Levison (2003)(*15*)
Tanzania	LIC	-	-	9-26%	150-669%	-	2004/2007	Antimalarials; interviews. Patouillard *et al.*(2010) (*99*)
Tanzania	LIC	-	-	48%+13% (2 wholesalers in chain)	100-233%	n	2003	Antimalarials; Battersby *et al.* (2003)(*116*)
Tanzania	LIC	-	-	27-56%	39-233%	-	2007	Antimalarials; interviews. Patouillard *et al.* (2010)(*99*)
Tanzania	LIC	-	-	18-41%	44-110%	-	2008	Antimalarials; interviews. Patouillard *et al.* (2010)(*99*)
Tanzania	LIC	16% (2.5% storage; 1% repackaging; 10% distribution; 2.5% administration)	0%	20%	30%	n	2004	Price survey report
Thailand	L-MIC	-	31 – 41% OB; 20 – 567% gen	0 - 1.6% OB; 6.7 – 31% gen	13 – 40% OB; 20 – 150% gen (includes tax)	n	2006	Price survey report

Thailand	L-MIC	-	15-30% scheduled; up to 400% observed	-	-	-	1998	More expensive products tended to have lower mark-ups but not consistent; methodology not robust. Pitaknetinan *et al.* (1999)(*84*)
Tunisia	L-MIC	10% (regulated)	0% (regulated)	8.7% (regulated)	31.6 – 42.9% regressive (regulated)	n	2004	Price survey report
Uganda	LIC	23% importer+0% LPG	0%	23% importer+2% OB; 6% importer+0% gen(imported); 4.2% gen (local) (10 – 40% stated)	364% OB; 403% imported gen; 233% local gen (36 – 720% stated)	n	2004	Price survey report
Uganda	LIC	-	-	27% (importer) + 29%	410-501%	n	2004	Antimalarials. Patouillard *et al.* (2010)(*99*) based on price survey report
Uganda	LIC	-	-	25-33% OB; 6-91% gen	28-365% OB; 30-720% gen	n	2004	HAI database: Importer and wholesaler mark-ups combined
Uganda	LIC	35%	-	(20-70% importer); 2-30% for imported or 15% for local	85-250% for imported; 105-145% for local	n	2007†	8 antimalarials and 5 other medicines; Auton *et al.* (2008)(*11*); Coughlan *et al.* (2008) (*25*)
Uganda	LIC	-	-	40-50%	38-100%	-	2007	Antimalarials; interviews. Patouillard *et al.* (2010)(*99*)
Uganda	LIC	-	-	-	40% ave. (ACT); 190% ave. (SP)	n	2007	RBM (2007)(*110*)
Ukraine	L-MIC	-	-	10-12%	up to 35%; up to 25% on some essential medicines (regulated)	n	2007	Price survey report
United Arab Emirates	HIC	-	-	20% (regulated)	20% (regulated)	n	2006	There have been reductions in mark-ups in recent times e.g. used to be 25% and 20% Price survey – HAI database

United Arab Emirates	HIC	-	-	See retail	Combined profit margin for agents and retailers in 3 categories: >AED500 = 25-35% AED300-500 = 35-45% <AED300 = 50% (regulated)	n	2005	Change introduced November 2005; not mark-up regulation; Anon (2007)(*118*)
Yemen	LIC	10% (regulated)	-	10% (regulated)	20% (regulated)	n	2006	Not enforced or CIF not updated? Price survey report
Zaire (DRC)	LIC	-	150%	-	-	n	1988	"profit margin' at self-financing health centres; Courtois & Dumoulin (1995)(*75*)
Zambia	LIC	-	-	-	29-67% (ACTs) 25-300% (SP)	n	2008	Clinton Foundation (2008)(*81*)
Zambia	LIC	-	-	-	30%	-	2003	Antimalarials; interviews. Patouillard *et al.* (2010)(*99*)

Key: *ACT: artemisinin combination therapy; Gen: generic; LPG: lowest priced generic; OB: originator brand; SP: sulfadoxine-pyrimethamine*
'Price survey' refers to surveys undertaken using the WHO/HAI methodology
* *Not publicly available at time of compilation*
† *Not survey using WHO/HAI methodology (although may have used it)*

Note: *Only WHO/HAI medicine price studies which had some data on mark-ups were included.*
Importer mark-ups not reliably captured (unless stated).
"Regulated" refers to some form of mark-up regulation. Even where mark-ups are not regulated, there may be other price regulation mechanisms.
Sources should be consulted for greater detail and explanation.

Appendix 5. Wholesale margins, retail margins and tax as a percentage of consumer price

	Distribution margins & taxes as % of consumer price (wholesale+retail+tax)	Wholesale margin (%)	Retail margin (%)	Tax (%)
Developed countries (Mossialos *et al.* 1994)(*118*)				
Belgium	43.4	8.5	29.2	5.7
Denmark	51.2	4.2	29.0	18.0
France	40.5	6.5	28.8	5.2
Germany	51.3	8.6	30.4	12.3
Ireland	42.1	8.8	33.3	0.0
Italy	38.5	7.3	22.9	8.3
Netherlands	41.2	11.8	23.7	5.7
Portugal	28.0	8.0	20.0	0.0
Spain	42.5	7.8	29.0	5.7
United Kingdom	42.5	7.5	35.0	0.0
Developing countries (WHO 1989)(*29*)				
Indonesia				
- Brand medicines	36.0	16.0	20.0	0.0
- Generic medicines	27.9	7.9	20.0	0.0

Source: Bennett et al. 1997 (*13*)

Appendix 6. Medicine retail price structures and overall costs in EU member states

Country	VAT (% price)	Retail (% price)	Wholesale (% price)	Manufacturer (% price)	Pharmaceutical expenditure (% GDP year)
Austria	16.7	24.1	7.5	51.8	1.3 (1999)
Belgium	5.7	29.2	8.5	56.6	1.4 (1997)
Denmark	20.0	23.4	4.1	52.5	0.8 (2000)
Finland	7.4	26.6	2.6	63.3	1.0 (2000)
France	5.2	26.2	3.8	64.8	1.9 (2000)
Germany	13.8	27.3	7.7	51.2	1.3 (1998)
Greece	7.4	24.0	5.5	63.1	1.5 (2000)
Ireland	0.0	33.0	10.1	57	0.6 (2000)
Italy	9.1	20.4	6.7	63.8	1.9 (2001)
Luxembourg	2.9	30.9	8.7	57.5	0.7 (1999)
Netherlands	5.7	20.2	10.8	63.4	1.0 (2000)
Portugal	4.8	19.0	8.4	67.8	2.0 (1998)
Spain	3.8	26.8	6.7	62.7	1.4 (1997)
Sweden	0.0	20.0	2.4	77.6	1.0 (1997)
UK	0.0	17.3	10.3	72.4	1.1 (1997)

Note: *Data represent the percent of final price.*

Based on data from Taylor et al. 2004 (19) origin Paterson et al. 2003 (24)

Appendix 7. Wholesale mark-ups - summary of mark-up regulatory strategies used in high-income countries

	Fixed fee (any format)	Reg'sive fixed fee	Fixed %age	Reg'sive %age	Cap?[†]	Notes
Albania	-	-	X	-	-	12%; lower on named high cost medicines
Australia [1]				X	Y	
Austria	X*	-	-	X	Y	*9-17.5% or a progressive fixed fee; Ave. wholesale margin 9%
Belgium	-	-	X*	-	Y	*13.1% up to €39 value thereafter 31% of first €24 plus low percentage on remainder
Bulgaria	-	-	-	X	Y	7-10%
Canada [1]	-	-	-	-	Y	Various mechanisms by region/plan
Cyprus	-	-	-	-	-	Unregulated. All imported medicine priced through international reference pricing; Fixed 20% for locally produced pharmaceuticals in private sector
Czech R. [1]			X		N	Total wholesale + retail mark-up of 29%
Denmark	-	-	-	-	N	Unregulated
Estonia	-	-	-	X	Y	3-20%
Finland	-	-	-	-	N	Unregulated; average margin 4%
France	-	-	-	X	N	Only reimbursed medicine; 2-10.3%
Germany	X*	-	-	X	Y	Fixed fee acts as cap to %age; 6-15%
Greece			X		N	8.43%
Hungary	X*	-		X	N	5-12%;
Iceland [1]			X		N	POM only
Ireland			X		N	15%
Italy			X		N	6.65%

Japan [1]					N	Unregulated

Korea [1]					N	Unregulated
Latvia				X		4-10%
Lithuania	X*			X	Y	Regressive 5.5-14% or progressive fixed fees acting as caps; Maximum mark-ups used
Luxembourg [1]			X		N	Domestic products only
Mexico [1]					N	Unregulated; However one citation that wholesale and retail margins are decided upon after negotiation between government and the manufacturer (US Dept. of Commerce 2004)
Netherlands [1]					N	Unregulated
New Zealand [1]			X		N	
Norway	-	-	-	-	N	Unregulated; ave. margin 5-7%
Poland			X		N	Max. mark-up; 9.8%
Portugal			X		N	18.25% of pharmacy retail price
Slovak R.				X	N	Max mark-up; 4-11%; only 2 categories (other special cases)
Spain [1]			X		Y	7.6%; Fixed fee is a cap to the fixed %age
Sweden	-	-	-	-	-	Unregulated; only 2 wholesalers with single channel distribution
Switzerland [1]	X			X	Y	Total wholesale + retail mark-up shared between distributors; Fixed fee + regressive percentage 8-15%
Turkey				X	N	2-9%
UK	-	-	-	-	N	Negotiated; nominal 12.5% total distribution margin
USA [1]	-	-	-	-	N	Unregulated

Note: *This table is based on the information available in the OECD report (7) and the PPRI report (21) and focuses on the pricing regimen used for public national health systems. However, it is not possible to capture the intricacies of the pricing strategies which may differ between public reimbursement systems and private sales, method of price caps and the like. Country PPRI reports should be consulted for these details.*

[1] From OECD (2008)
[†] If there is a maximum value above which the mark-up should not exceed. This is not the same as having a maximum percentage mark-up.
Some flat fees may be regressive in nature.
"Unregulated" means there is no set mark-up; regulations may still exist as part of price regulation

Appendix 8. Retail mark-ups - summary of mark-up regulatory strategies used in high-income countries

	Fixed fee (any format)	Reg'sive fixed fee	Fixed %age	Reg'sive %age	Cap?†	Disp. Fee?	Notes
Albania	-	-	X	-	N	N	29%; lower on selected high cost medicines
Australia [1]	-	-	-	X	Y	Y	
Austria	X*	-	-	X	N	Y	3.9-37% or a progressive fixed fee; Disp. Fee only for private clients; ave. retail margin 20%
Belgium	-	-	X*	-	Y	N	*31% up to €39 value thereafter 31% of first €24 plus low percentage on remainder
Bulgaria	-	-	-	X	Y	N	7-10%
Canada [1]	-	-	-	-	-	-	Various mechanisms by region/plan
Cyprus	-	-	-	-	-	-	38% in private sector
Czech R. [1]					N	N	Total wholesale + retail mark-up 29%
Denmark	X*	-	X*	-	N	Y	*progressive fixed fees and regressive factors built into formula; 55%
Estonia	X	-	-	X	Y	N	0-40%; fixed fee not applied in all cases; higher fixed fee for most expensive products
Finland	X*	-	-	X	N	Y	12.5-50% plus *progressive fixed fee
France	-	-	-	X	N	Y	Only reimbursed medicines; 6-26.1%
Germany	X**	-	X	-	Y	Y	3% (plus €8.10 per package)
Greece	-	-	X	-	N	N	35%
Hungary	X*	-	-	X	Y	N	17-26%; *progressive fixed fee
Iceland [1]	-	-	X	-	N	-	POM only
Ireland	-	-	-	-	N	Y	Not officially regulated but agreements exist; 50% plus dispensing fee
Italy	-	-	X	-	N	N	Statutory discount creates regressive margin

Japan [1]					N	Y	Unregulated
Korea [1]					N	Y	Unregulated
Latvia	X*	-	-	X	N	N	*Formula incorporates regressive percentage and progressive fixed fee
Lithuania	X*	-	-	X	Y	N	Regressive 4-22% or progressive fixed fees acting as caps; Maximum mark-ups used
Luxembourg [1]			X		N	-	
Mexico [1]					N	-	Unregulated; However one citation that wholesale and retail margins are decided upon after negotiation between government and the manufacturer (US Dept. of Commerce 2004)
Netherlands [1]			X		Y	Y	
New Zealand [1]				X	N	Y	
Norway	X**	-	-	X	N	Y	Max mark-ups; 5-8%; fixed fee could be considered dispensing fee
Poland	X*	-	-	X	Y	N	Max mark-ups; 12-40% or progressive fixed fee; fixed fee acts as cap
Portugal	-	-	X		N	N	18.25% of pharmacy retail price
Slovak R.	-	-		X	N	Y	10-21%; only 2 categories; other special cases
Spain	-	-	X		Y	N	27.9%; Fixed fee is a cap to the fixed %age
Sweden	X*	-	-	X	Y	N	0-20% regressive %age plus a progressive fixed fee; capped since highest category get 0%
Switzerland [1]	X			X	Y	Y	Total wholesale + retail mark-up
Turkey	-	-	-	X	N	N	10-25%
UK	-	-	-	-	N	Y	Not regulated directly but target margin monitored
USA [1]	-	-	-	-	N	N	Unregulated

Note: *This table is based on the information available in the OECD report (6) and the PPRI report (21) and focuses on the pricing regimen used for national health systems. However, it is not possible to capture the intricacies of the pricing strategies which may differ between public reimbursement systems and private sales, method of price caps and the like. Country PPRI reports should be consulted for these details.*

[1] From OECD (2008)(7)
[†]If there is a maximum value above which the mark-up should not exceed. This is not the same as having a maximum percentage mark-up.
Some flat fees may be regressive in nature. Difference between a fixed fee and a dispensing fee at retail level not always clear (e.g. Germany, Norway).
"Unregulated" means there is no regulated mark-up; regulations may still exist as part of price regulation

Appendix 9. The presence of discounts and rebates in the EU pharmaceutical sector

Country	Discounts/rebates
Albania (2009)	No discounts/rebates allowed – prices fixed.
Austria (2008)	Pharmacies pay a 2.5% rebate to sickness funds; other pay-back mechanisms possible. Dispensing doctors not permitted to receive rebates in kind but can receive cash rebates. Hospitals receive rebates in kind from pharmaceutical companies.
Belgium (2008)	No statutory discounts/rebates. No discounts/rebates allowed – prices fixed.
Bulgaria	No regulation. May be in cash or in kind.
Czech Republic	-
Cyprus	No regulation. May be in cash or in kind from wholesaler to pharmacy. Private hospitals may receive discounts from pharmacies.
Denmark	Manufacturers/importers may grant wholesalers discounts. Wholesalers may grant pharmacies discounts but they are regulated, must be published and available to all retailers.
Estonia	No statutory discounts/rebates. Commercial discounts allowable and not regulated.
Finland	Manufacturers/importers may grant wholesalers discounts. Discounts may not be granted to pharmacies which have fixed prices.
France (2008)	Discounts/rebates of pharmacy purchase price negotiated with suppliers and are regulated. Reimbursable originator brands: max. 2.5% Reimbursable generics (and off-patent): max 17% of ex-factory price Non-reimbursable medicines: not regulated
Germany (2008)	A number of legislated 'forced' rebates to be paid by manufacturers and pharmacies to sickness funds based on patent and prescription status of the medicine which are matched with set manufacturer prices to prevent these being offset by increased prices. Also negotiated rebates between pharmaceutical providers and sickness funds, and commercial rebates between pharmaceutical providers.
Greece	Discounts are strictly regulated and can be given on certain circumstances. • 5% discount from wholesalers to pharmacists • 4% for pharmacists in small towns • Unlimited discounts can be given to public hospitals

Hungary	No statutory discounts and no regulations. Price-volume agreements possible between manufacturers and national health insurance fund.
Ireland	No statutory discounts but 3.53% rebate on General Medical Services sales must be paid to Health Service Executive Discounts for timely payments common; no information on discounts made to hospitals or pharmacies.
Italy	Statutory regressive discounts for pharmacies depending on urban/rural location and national health service turnover. Commercial discounts/rebates allowed in the hospital sector but are regulated. Possible other discounts/rebates from manufacturers.
Latvia (2008)	No discounts/rebates allowed.
Lithuania (2008)	No statutory discounts/rebates. Commercial discounts allowable and not regulated.
Luxembourg	-
Malta	-
Netherlands	-
Norway (2008)	Price regulations set maximum prices and discounts/rebates are allowed although unlikely other than in the hospital sector where they average 31%.
Poland	No statutory discounts/rebates. Cash discounts/rebates not allowed for reimbursable medicines. Natural rebates (rebates in kind) are allowed. Maximum mark-ups allow for discounts
Portugal (2008)	Ministry of Health and manufacturers negotiate rebates in case of public pharmaceutical over expenditure. Commercial discounts allowed at all levels. Pharmacy discounts may only be in the patient co-payment.
Slovakia	No discounts/rebates allowed.
Slovenia	-
Spain	-
Sweden	None – prices fixed, although city councils are given discounts for medicines used in hospitals
Turkey	Public sector statutory discount applied at time of pricing at manufacturer (4% and 11% for originator products with up to 6 years or more than 6 years on the market; 11% for generics) and pharmacy level (3-4.5% depending on turnover). Commercial discounts allowable and not regulated.
United Kingdom	Commercial discounts allowable through price negotiations with claw-back mechanism for reimbursed medicines.

Note: *Information summarised from PPRI country reports (2007 unless otherwise stated). The above summaries should not be taken in isolation, but understood within the form of price regulation in force in the particular country. Information may not be complete and may concentrate on public provision of prescription or reimbursed medicines. Pharmaceutical sales to private institutions or for private sale may not be subject to the same regulation as national health service or insurance services. The reader is directed to the PPRI country reports for more details. (http://ppri.oebig.at/)*

Appendix 10. Pharmacist remuneration models for prescribed medicines

Country	Business margin	Fixed or regressive mark-up/margin	Fixed dispensing fee	Service fee	Capitation
Australia		X	X	X	
Austria		X			
Belgium		X		X	
Brazil	X				
Bulgaria		X			
Canada	X		X	X	
Cyprus		X			
Czech Rep.		X			
Denmark		X	X	X	
Estonia		X			
Finland		X	X		
France		X	X		
Germany		X	X	X	
Greece		X			
Hungary		X			
Iceland		X			
Iraq	X				
Ireland		X	X	X	
Italy		X			
Japan	X		X		
Jordan	X				
Korea (Rep. of)	X		X		
Kuwait		X*			
Latvia		X			

Lithuania		X			
Luxembourg		X			
Mexico	X				
Netherlands		X	X		X
New Zealand		X	X		
Norway		X	X		
Peru		X			
Poland		X			
Portugal		X		X	
Saudi Arabia		X			
Slovenia			X		
Slovak Rep.		X	X		
Spain		X			
Syria	X				
Sweden		X			
Switzerland		X		X	
Turkey		X			
United Kingdom	X		X	X	
United States	X		X	X	

** Blank in the original table*

Source: Bernsten *et al*. 2009 (*45*)

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