Global framework for differential pricing of pharmaceuticals

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GLOBAL FRAMEWORK FOR DIFFERENTIAL PRICING OF PHARMACEUTICALS

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ABSTRACT

This paper examines how equitable, differentiated pricing can improve access to and affordability of medicines, particularly in low- and middle-income countries, and how governments and supranational agencies can create an environment that enables pharmaceutical companies to operate a sustainable business model benefitting all key stakeholders. Using value-based pricing techniques in combination with a non-linear function that captures national income parameters as defined in the Human Development Index together with health system variables, the authors have developed an integrated pricing policy framework. The degree to which the proposed framework offers a sustainable solution to the problem of access to medicines depends on: the economic development status of a country, the value of a particular medicine to its therapeutic class and the incidence of the relevant disease, and the extent to which market segmentation can be applied. This paper further argues that for equitable, differential pricing to succeed, policymakers and lawmakers must design and implement a regulatory and legislative framework that prevents leakage through parallel trade and price referencing between affluent and poorer segments when discounts are applied.

Key words: globalization, pharmaceuticals, public policy, corporate strategy, pricing, access, equity.

JEL: D430, L110, L650.

1. INTRODUCTION

Medicines prevent and treat diseases, enabling people to live longer, healthier and more productive lives and contributing significantly to social and economic advances. Consequently, access to medicines is the cornerstone of any meaningful public health and development policy. Yet, achieving global access remains a challenge. Worldwide, communicable and non-communicable diseases continue to place an enormous social and economic burden on societies. For example, lifestyle changes and an ageing population in developed as well as in developing countries are contributing to new epidemics in non-communicable diseases, such as diabetes, while ever increasing global travel, trade, migration and climate change are likely to accelerate the transmission of infectious diseases within communities and beyond. Against this backdrop, the quest for new and improved treatment, prevention and cure continues relentlessly. Arguably, the greatest challenge for public policymakers and corporate executives is to secure the availability of affordable drugs and health technologies, without restricting the innovative capacity of science and technology driven public organizations and private firms. Both sides – affordability and innovation – of the equation must be satisfied to secure a steady stream of new medicines.

Action is required on many fronts to address this multifaceted problem. According to public health experts including the World Health Organization (WHO), access to medicines depends primarily on availability (supply), affordability (income), adoption (uptake), and appropriate use (particularly in the field of infectious diseases where drug resistance is always a looming threat). These critical determinants are known as the 4A's. Because they are dynamically inter-linked, it is difficult to identify which of the 4A's should be first dealt with in order to achieve the greatest possible benefit. In this paper, the authors address the relationship between affordability and pricing of medicines, and in particular pharmaceuticals, by presenting a practical integrated policy framework and analytical model for policymakers and executives to design equitable, transparent and systematic pricing strategies.

This paper also focuses on the widespread debate about the respective roles of government, business and civil society triggered by the concern about access to medicines and the related affordability and pricing questions. A recent editorial by the Lancet asserts that 'companies must be better held to publicly account in relation to those responsibilities' (D. Molyneux, 2010). In other words, pharmaceutical and biotechnology companies that invent, manufacture and supply health-related products have the responsibility to improve access to health care to their products. Similarly, the United Nations Human Rights Report (UN Human Rights Report) emphasizes that companies should take all reasonable steps to make life-saving medicine as widely accessible as possible. The *Working Group on Access to Essential Medicines*, convened by the United Nations, also recommends that the main actors involved in the supply of pharmaceuticals, find new ways to interact, so as to ensure that needed medicines are available (Leach B., Paluzzi J., Munderi P., 2005).

Given that health is considered a human right, access to medicines is high on the agenda of both public and private stakeholders. Failure to respond in a timely or appropriate fashion to this issue can therefore harm the firm's reputation. In some instances it has already led to more stringent regulation; including compulsory licensing. As a result pharmaceutical companies are being urged to publicly take their responsibilities 'to the maximum of available resources' as states do. Evidently,

more will be required of a powerful transnational company with global networks, than of smaller businesses.

Not surprisingly, the debate about the respective roles of government, business and civil society in improving access has provoked polarized views. While some scholars suggest that the purpose of a firm is to first and foremost make profit; their critics argue that distributive justice should prevail. Thus on one side of the spectrum are those who claim that, to borrow Milton Friedman's phrase, 'the-business-of-business-is-business'. On the other side are patient groups, civil society, politicians and increasingly the firm's own stockholders who emphasize the ethical importance of the issue of access to medicines. An increasing number of citizens also have come to expect business to assume a greater responsibility in society. In that context, various scholars have attempted to not only define corporate social responsibility (CSR) as a concept under the wider umbrella of good governance, but also as a strategy to create a potentially sustainable competitive advantage. Even though an increasing number of firms claim that they adhere to the principles of CSR, sceptical advocacy groups argue that they must go further in their social commitment. The question is how to reconcile these philosophically contrasting viewpoints?

This paper argues that a sustainable solution to access to and affordability of medicines goes beyond CSR and forms an integral part of corporate strategy. We propose that corporations establish *inter alia* a differential pricing policy across various population segments in response to the wide-ranging differences in socioeconomic background and related buying power. By making its products available to a wider range of citizens, and taking into account the inequality in wealth and income, the firm is in effect applying the principle of equity to pricing and simultaneously achieving both business and social contract objectives. For a pharmaceutical firm to realize these twin goals, and particularly for those endeavouring to make new and existing products more accessible to all who need them, we recommend that they use all the instruments at their disposal and adopt a fundamental and structural approach. This include differential pricing between countries with different income levels (with the intention to bridge the disparity between rich and poor countries), differential pricing within the same nation (by applying intra-country market segmentation), and through non-exclusive commercial voluntary licenses, non-commercial voluntary licenses, donation programmes, and public-private partnerships.

This study demonstrates that adapting prices of pharmaceuticals to the purchasing power of patients and consumers in different geographical or socioeconomic segments is an effective way to improve access to and affordability of life-saving medicines in the short as well as the long term. The integrated differential pricing framework and decision-analytic model presented herein is expected to facilitate better and faster access to medicines, especially for people living in low-income and middle-income countries. The proposed conceptual framework also aims at finding a balance between achieving greater equity in pharmaceutical access while preserving incentives for research and development of future medicines to address the unmet medical needs of tomorrow. It is argued that non-linear regression analysis incorporating human development index parameters provides a proxy for the ability-to-pay and for calculating the corresponding 'equity' discount levels. In addition, the model may serve as the basis for bilateral price-volume negotiations.

The paper is divided into six parts. Part one briefly introduces the problem; part two discusses the issues and parameters encountered in setting pharmaceutical prices and the dynamics currently

shaping prescription drug economics; part three describes a conceptual framework and analytic model for differential pricing in the global economy; part four identifies intra-country opportunities for differential pricing; part five analyses various public policies aimed at fostering an enabling environment; and part six summarizes the discourse and sums up the key findings and recommendations.

2. The Current Reality of Pricing Pharmaceutical Goods

The law of supply and demand applies to pricing strategy for the majority of goods. In general, if the price of a particular good is set at a lower level than the real or perceived value to the consumer, a shortage will occur and the price will gradually rise. Conversely, if the price is considered higher than its value to the consumer, a supply surplus results and the price declines. Eventually, equilibrium is reached, meaning that the supply and demand curves intersect at the point at which the quantity demanded by the consumer equals the quantity supplied by producers. The price that corresponds to this market-clearing point is considered to be the correct unit price for the particular good. Underlying the above logic are the principles that: 1) information is freely available to enable the consumer to evaluate the good, and 2) the consumer has the ability to choose whether or not to purchase the good, or service.

In contrast to other consumer goods, the relationship between supply and demand in the market for pharmaceutical products is different. First, there is asymmetric information between the principal (i.e. patient), and his/her agent (i.e. prescribing doctor). Second, the market for pharmaceuticals is generally less price sensitive in comparison to less essential goods. This is illustrated by the following statement: "a sick patient does not have 'consumer sovereignty' to buy or reject a [medical] product" (Kumra, 2006). For example, if you need transport, you often have the options of purchasing a car or a bicycle or of taking public transport; if you are sick, however, you need a medicine, and if it is lifesaving you have even less choice. Third, over time, the decision about which product to use has been transferred gradually from the physician to the insurer and/or payer. As a result, the configuration between the various actors and their respective decision-making power with regard to pharmaceuticals can be summarized as follows: the physician prescribes, the patient consumes, and the government or insurance company pays. For that reason it is no surprise that the latter will try to contain costs. The danger is that this restriction on willingness to pay comes at the expense of achieving the appropriate balance between industry incentive and societal reward.

A third factor is that pharmaceuticals and other medicines are considered by many to be a public good. In light of the nature of the product, they are highly regulated. Government regulations concern, among other aspects, product safety, clinical testing, generic substitution, coverage under national health insurance plans or national formulary system, patent protection, compulsory out-licensing, and R&D incentives. Today, with society becoming increasingly risk averse the regulation with the greatest impact on new pharmaceutical development is that of mandatory pre-clinical and clinical testing. This, combined with the associated soaring research and development (R&D) costs and downward pressure on market prices, make it increasingly difficult for many pharmaceutical companies to recoup R&D expenditures before the patent expires. As a result, to be profitable innovators and manufacturers of pharmaceuticals must carefully manage costs throughout the value chain and develop products that are highly valued by society and either address unmet needs or ensure a competitive edge. In other words, regardless of whether the price of a medicine is reasonable or unreasonable from the point of view of the supplier, the medicine will not be purchased or used if the patient or the health system cannot afford it. Price is a demand factor.

Within this context, there appear to be two major confines between which an optimal price must be determined: on the one hand, the R&D and general production costs of the product; and, on the other the purchasers and consumers' formal or informal valuation of the product based on an

assessment of its social, economic and personal usefulness. The first aspect influences the supply-side costs, while the second deals with attempts by buyers to control demand-side aspects. What follows is a brief overview of the issues encountered and how they influence the buyer-seller relationship.

On the supply side, innovation in the pharmaceutical industry is notorious for being complex, lengthy, costly, and risky. It is estimated, for example, that the cost to develop a new medicine ranges from US$ 500 million to US$ 2 billion, depending upon the targeted disease, and requires an average investment time of 73 months. Even more daunting, only 20% of potential drugs are ever brought to market (Adams and Brantner, 2006). Consequently pharmaceutical firms argue that these *sunk costs* must be fully recouped by the 20% of medicines that make it to the market and are actually sold. In addition, pharmaceutical prices are affected on the supply side by generic manufacturing firms which successfully produce medicines shortly after the patents expire and avoid the R&D and marketing expenditures. The effect upon life-cycle pricing can be quite dramatic. To compensate for the generic firms' cost advantages and to continue funding R&D at the levels discussed above, original manufacturers argue that they must achieve extraordinary profits during the patent life of a new compound. If all of these cumulative costs were to be passed on to the consumer, invariably prices would be high thus forcing the poor and uninsured out of the market. We discuss ways to offset part of the above fixed cost in part 3 and as a result address the inequity caused by market failure.

At the same time, on the demand side, due to the pressure on health care budgets, every government or third-party payer is eager to control increasing expenses through the implementation of central cost containment policies, particularly in relation to pharmaceuticals. For both governments and third party payers obtaining value for money from use of pharmaceuticals is a key policy objective because it is important in maximising the health gain derived from public and private resources. A range of pharmaceutical cost containment policies exists, comprising generic substitution, patient co-payment, and price control (López-Casasnovas, G., Jönsson, B. (eds.) (2001).

Two policies which have become very popular in recent years are: reference pricing within a particular therapeutic group, and health technology assessment (HTA). Experts agree that compared with HTA, reference pricing is a relatively inefficient instrument for obtaining value for money from pharmaceuticals (Drummond et al., 2011). Under a system of *internal* reference pricing, pharmaceuticals that are judged to be similar are clustered and a single level of reimbursement (i.e. the reference price) is set for the entire therapeutic cluster, usually based on the price of the cheapest drug or vaccine in that group, or on some average of existing prices. It is important to note that this type of reference pricing takes place within the same (reimbursement) jurisdiction, and is not to be confounded with the international price referencing where prices for the same product are compared across various countries and population groups with different income levels (GDP) and purchasing power. We will discuss this in part 3.

An increasing number of industrialized (OECD) countries, such as the United States (US), Canada, Germany, United Kingdom (UK) and Australia utilize HTA in their pharmaceutical pricing and reimbursement decisions. Despite this experience and national and international guidelines for the HTA methodology, hurdles related to methodology, resources, transparency of information and scope remain. HTA studies continue to be conducted using different methods, representing varying

viewpoints which affects the measurement and valuation of costs and consequences. In health economic and pharmaco-economic evaluations, the most widely used viewpoints are that of the patient, health care professional, health care institution, third-party payer, pharmaceutical industry, and employer. HTA evaluations also can be very resource intensive, if performed correctly. This then limits their use in developing countries, many of which do not yet have the necessary resources or institutional capacity. A further complication is the imperfect transparent information on pricing and reimbursement decisions because authorities are not always obliged to make these public (Oehlrich, 2011). Thus, it is hard to compare HTA evaluation and health economic data and decisions between countries, and if health care budgets remain decentralized, it is difficult to compare even within the same region.

Despite these hurdles, HTA is considered by many to be a useful tool in supporting value-based pricing decisions for pharmaceuticals. At the very least, HTA helps purchasers and consumers make informed decisions by judiciously analysing the different options available in treatment, diagnosis, and prevention. Reimbursement is usually granted if the incremental cost-effectiveness ratio obtained by comparing the product under investigation with other relevant alternatives falls within an acceptable range. There is controversy about the cut-off point at which programmes can be considered cost-effective. The countries that refer to HTA studies generally use 'thresholds' that are directly or indirectly linked with willingness and ability of the payer to pay. By setting a threshold on the price per unit of health gain, or cost-effectiveness ratio, as a condition for reimbursement, the payer expresses her willingness to pay with regard to the value offered. For example, the UK's National Institute for Health and Clinical Excellence (NICE) estimates the additional life years and quality of life gained by using the new product, as well as the product's additional cost as a treatment or prevention technique. The ratio of extra cost to extra benefit is then expressed as a cost per quality-adjusted life-year gained. If the ratio is below the Institute's threshold of $33,000-$50,000, it recommends the product for use.

HTA does not however address equity, nor can it be used to set guidelines on how much nations should spend on pharmaceutical care. In the next sections we will investigate whether additional or supplementary methods can be used to measure *ability-to-pay* at the macro (nation), mezzo (health system), and micro (individual) level.

3. Building A Global Framework For Differential Pricing

3.1 The Power of Differential Pricing

This section argues that differential pricing is a very effective strategy to improve access to medicines in low and middle income countries, as well as in low-income communities within high-income countries. Differential pricing is in essence the adaptation of product prices to the purchasing power of patient-consumers (who are usually represented by procurement agencies and third party payers). There is clear evidence that differential pricing can result in a win-win both for consumers, enhancing their social welfare, and for industry, where a well implemented differential pricing strategy leads to incremental sales. The reality is that manufacturers do not always know the individual consumer's willingness to pay, but they are able to roughly categorize consumers according to their respective level of income.

Differential pricing (occasionally called tiered pricing or economic price discrimination) is well established across various industries (e.g. airlines, energy, etc.). As described by Danzon (2003, 1997), Towse (2007), Prashant (2010), Barton (2001), a differential pricing strategy works particularly well for pharmaceutical products (including drugs, vaccines and diagnostics) because the relatively high investments in fixed assets or R&D over a 15-20 year period can be considered a 'global joint cost' that benefits consumers worldwide. Moreover, Szymanski and Valetti (2005) and Valetti and Szymanski (2006) have shown that differential pricing permits a higher level of R&D than would otherwise occur under uniform pricing and leads to more appropriate use of medicines than does uniform 'flat' pricing.

The economic theory underlying pricing to cover joint costs is called Ramsey pricing. By and large, Ramsey pricing seeks to identify the price that provides the highest social benefit to consumers, while also generating sufficient revenues to cover the costs, including joint costs (Laffont et al., 1993; Baumol et al., 1970; Ramsey, 1927). Accordingly, the mark-up of a price over its marginal cost should be greater for consumers who are relatively price-insensitive (inelastic demand) than for consumers who are more price sensitive (elastic demand). The price differential leads each group to reduce its respective demand by an equal percentage relative to the hypothetical demand at a price equal to the marginal cost. If everyone were charged the same uniform price, the price sensitive consumers would decrease their consumption and thus experience a greater loss in welfare than the price insensitive consumers. Consumers, who are highly price sensitive, as are the majority of citizens living in low-income countries, may entirely drop out of the market, even though they might have been willing to pay a price high enough to cover the marginal cost of manufacturing the product (i.e. excluding its fixed R&D cost).

While Malueg and Schwartz (1994) contend that economic price discrimination is both profit-maximizing and welfare-superior to uniform pricing, Danzon and Towse (2003) defined the necessary conditions for efficiency in pharmaceutical utilization and product development: (1) price *P* is at least equal to marginal cost *MC* in each market or country; and (2) prices exceed *MC* by enough, in aggregate over all markets, to cover joint cost of R&D, including a normal, risk-adjusted rate of return on capital (F):

$P_j \geq MC_j$, and

$$\sum(P_j - MC_j) \geq F$$

Ramsey optimal pricing implies that social welfare can be enhanced by applying differential pricing across cohorts of different income levels. Accordingly prices should differ across different market segments in inverse relationship to their demand elasticity. In the case of a single product, the condition for the optimal mark-up of price over marginal cost for submarket j can be described as follows:

$$L^j = D / E_j$$

In line with this theory, Lj, which is the mark-up of price over marginal cost (also called the Lerner index) in sub-market j, should be proportional to the demand elasticity Ej. Likewise, the proportionality term D is defined by the specified target profit level for the producer. Under Ramsey optimal pricing, price-sensitive users should be charged a smaller mark-up over marginal cost than less price-sensitive users, because the price sensitive users would reduce their consumption by proportionately more, if faced with the same prices. Charging lower prices to more price-sensitive users is consistent with equity, assuming that lower income consumers have more elastic demand, on average.

Differential pricing is therefore a prime example of equitable pricing. Whereas the term differential pricing stems from business economics, the term equitable pricing is derived from social welfare concepts. The point is that these two schools of thought go hand-in-hand and in fact are mirror images of each other; as illustrated in figure 1. To improve access to medicines worldwide, it is critical for manufacturers to be able to offer less affluent countries lower prices. At the same time, innovators and manufacturers must recover their costs whilst earning a fair return on their investment so as to support continued investment in R&D and scale up of production capacity. This delicate balance can be attained by amortizing expenses *unequally* across countries such that poorer countries pay a relatively lower price, but nonetheless *equitable* share for their products compared to more affluent countries. Consequently, differential pricing can result in significant progress in access to medicines in both affluent and less economically developed countries. In addition, the principle of differential pricing is applicable to medicines for treatment of a range of diseases, not only those confined to poor countries. Section 5.5 briefly describes the supplementary incentives that must be created to promote R&D of medicines of interest to developing countries (and for which differential pricing is impossible or insufficient).

The most difficult trade-off in pharmaceutical policy is the seemingly inherent one between static efficiency – where consumer welfare is maximized by obtaining the highest health value from today's expenditures at the lowest cost possible – and dynamic efficiency, where R&D incentives grow the capacity to prevent, cure and perhaps eradicate diseases in the future. The dilemma is that obtaining the best possible price or lowest possible expenditure for pharmaceutical products in today's market may mean having fewer and less innovative alternatives in the future. The associated pricing policies are diametrically opposed with static efficacy demanding relatively low prices, and dynamic efficacy requiring a price premium to stimulate innovation. By addressing both of these conditions simultaneously, differential pricing leads to an optimal policy for pricing and access that benefits all stakeholders, something flat pricing cannot accomplish. This is illustrated in figure 2. Unfortunately, the public perception is that such price differentials imply cost shifting from low-price to high-price markets. Statements such as 'a pharmaceutical company may only be willing to sell in a

low-income country because it can recoup any losses it incurs there from sales in high-income countries' may create controversy. In fact consumers in affluent markets are not necessarily being charged artificially higher prices because they would have paid for the good anyway. These statements either ignore the 'jointness of R&D costs' inherently linked to inventing and producing pharmaceuticals, or mistakenly assumes that all consumers should contribute equally, contrary to welfare-maximization principles. By the same token differential pricing should not be labelled a 'subsidy' (Plahte, 2005) as doing so can mislead policymakers to discourage the use of a mechanism that in effect benefits all stakeholders.

3.2 Gross Domestic Product and Development Indicators

As noted earlier, differential pricing inherently includes the notion of equity and has a redistributive effect. The pertinent remaining question is who should pay what share of the R&D costs incurred? Because the 'global joint cost' of inventing and manufacturing medicines cannot be attributed to a particular group of consumers or country, the cost structure by itself cannot determine the proportion each country or beneficiary should contribute. In this section, we argue that a country's gross domestic product, or its ranking in the Human Development Index (HDI), provides an adequate measure, and perhaps more importantly a more objective and verifiable benchmark. Adding these two variables to the evaluation process broadens the arsenal of proxy measures to assess ability-to-pay.

While use of the gross domestic product (GDP per capita) of a country as a parameter in differential pricing was mentioned briefly in discussions surrounding the WHO conference on differential pricing and financing of essential drugs (WHO, WTO, 2001), there has been no further debate on how to calculate this or comparable parameters and how to use the outcome in equitable pricing decisions. We propose to adopt a philosophy similar to the one advocated in the Human Development Reports (1990 to 2010). The HDI[1] is calculated as a composite index comprised of the sum of three individual indices - income index, education, and life expectancy; each representing one third of the total. While education and life expectancy represent linear functions, the income index is the logarithm of income for a country. By definition it is positioned between two extreme values marking the minimum and maximum goalposts (i.e. that year's country with the highest income, and the country with the lowest income). Between these two extremes, all other countries are ranked using annually published data from the World Bank. The rationale for using this logarithmic formula to indicate income and ability-to-pay is that 'income must be adjusted to reflect a decent standard of living; and achieving a respectable level of human development does not require unlimited income'. Whereas the Human Development Report uses purchasing power adjusted GDP per capita (PPP US$) to calculate the income index, we recommend using the purchasing power parity (PPP) adjusted Gross National Income (GNI) per capita because gross national income instead of gross domestic product (PPP adjusted) for any particular country provides a more refined picture of the nation's true wealth.

Figure 3 plots the logarithmic function of GNI per capita (PPP) for a selection of 128 countries worldwide, resulting in a non-linear regression curve. The countries (World Bank listings; not all shown) are ranked on the X-axis according to their national income, with the poorest countries to the left and the richest to the right. The resulting *equity curve* is a graphic representation of the concept of a price index calculated based on the country's national income. The steepest discounts

[1] See technical notes section of the 2007/2008 report.

are reserved for the poorest countries, while for middle and high-income countries the discounts are expected to gradually decrease as the country's wealth increases, leading to standard prices (without further 'equity' discounting). The degree of discounting can be illustrated by a slope drawn at each point of the price index curve (not displayed). To translate this 'price index curve' into real prices for any specific product the same logarithmic function of income (GNI per capita, PPP) as described above is used at the beginning to draw a product price equity curve. This curve translates the 'price index curve' into real prices for a particular product. One can define one high-income country as the maximum goalpost, or calculate the median of eight to ten high-income countries. A price point is defined for that one country or basket of countries. Beginning from this benchmark the extrapolation is reflected in a product price equity curve. It is expected that the reference country will substantiate its competitive profile and price potential based on hard product data and value (using value-based pricing and HTA techniques). The authors advise to use the United States GNI per capita as a reference value in pricing scenario analyses, as it is a country with one of the highest incomes per capita and has a well documented value-based pricing policy. Alternatively, the median of the top ten OECD countries could be used as the reference or anchor point as well, but in doing so the income level and health care systems of the countries chosen must be comparable for the anchor value to be representative.

The above rationale makes sense intuitively from an equity perspective. If today's highly developed economies like the US, Europe and Japan find the cost of a medicine or health-related technology to be a burden; certainly low-income countries will experience a relatively greater and heavier financial burden due to the preponderance of poverty among their populations. The curve implicitly shows how the 'global joint costs' of product R&D, including clinical trials, and those associated with the construction of large-scale manufacturing plants, obtaining regulatory approval, and paying liability insurance fees, among others, can be distributed proportionally across different consumer groups, and in accordance with their respective financial means. Application of this rationale at the aggregate country level permits a higher-than-marginal-cost price for well-off consumers, who thus absorb a substantial proportion of fixed costs. For the less affluent consumers, the price gradually declines, so that on average less fortunate consumers face a cost closer to the marginal costs of production, marketing and distribution. For the poorest countries, a special effort must be made as they may not be able to afford any price, no matter how low the marginal production cost may fall (through economies of scale, licensing third parties, or outsourcing to low-income countries). For these countries, there must be an international subsidy, financed through a mixture of multilateral development aid and philanthropy.

In Figure 3, different cost bearing levels can be observed in three groups: 1) industrialized countries, 2) innovative emerging economies and 3) high-burden resource-poor countries. Emerging economies occupy a special position on the curve, especially in comparison with the HDI data curve. If evaluated both by their national income and HDI, the emerging markets undeniably have the capacity to absorb a considerable part of product development and production costs, even at the present time. They should not be allowed to free ride. That is, not all of the fixed cost burden should be, or perhaps even cannot be, shouldered by the cohort of high-income countries (while this is overwhelmingly the case at present). Indeed, the world economy is rapidly changing and therefore a modification in policy and practice is needed. Two opposing future trends are likely (Rodrik, 2011; The Economist, 2011): (i) The United States and Europe struggle on as wounded giants, suffering the repercussions of their financial excesses and political paralysis. They seem condemned by their

heavy debt burdens to years of stagnation or slow growth, widening inequality, and possible social strife; (ii) meanwhile, much of the rest of the world is brimming with energy and hope. Policymakers in China, Brazil, India, and Turkey are concerned about too much, rather than too little growth. Perhaps for the first time in modern history, the future of the global economy lies in the hands of developing countries and emerging markets. We will discuss the consequences of this shift and the impact of emerging markets on pricing in section 3.3.

From the beginning our objective has been to create an analytic model that enables executives to determine the equity level in pricing across markets. The proposed model measures the degree of 'equity' that will eventually guide 'policy' making and implementation. As part of this process, it is also important to consider pricing in the context of volume. Figure 4 shows the relationship between price based on net sales data and product volume (number of doses) and the theoretical equitable price for a hypothetical drug. Given that each compound has a specific and unique context firms will need to assess how realistic the outcome of their pricing policy is by carefully interpreting the potential deviations between the theoretical price equity curve (full regression curve) and real sales data curve (dotted regression curve). The size of the bubble reflects the volume sold in that respective country. Depending on the therapeutic area, and often also on the incidence and burden of the disease, additional concessionary prices can be granted, usually on a case by case basis. In any event, prices are unlikely to decline in the absence of volume guarantees. Especially in low and middle-income markets, product forecasts are highly variable and volumes, even if they are stipulated in supply contracts, may fall short of initial expectations, while price discounts remain valid. In this scenario, discount rates based on volume gains may need to be considered. Here too, the relationship between price and volume is non-linear. For instance, if the firm is to maintain its profit margin, let alone grow the business through geographic expansion and achieving higher consumer coverage, a price reduction of 10% may have to be compensated by a volume increase of 25%. Methods for calculating price-volume trade-offs are beyond the scope of this article, and are described in the literature (Nagel, Holden, 1995; Monroe, 1990).

The model offers corporate management a powerful tool to test the company's own 'equity' profile. In utilizing it, corporate management should consider that while Figure 3 suggests that 'equitable' prices are correlated with national income levels and that price levels can be calculated using a nonlinear regression analysis, the GNI per capita (PPP) data are based on published 'nominal' values. Therefore the model generates a 'theoretical' price index, not the actual 'market' price for pharmaceuticals. The latter likely reflects several factors outside of the model. Regardless of their geographic operations companies can only control *ex-factory* price-setting for their own products and guidelines within their own jurisdiction. Consequently, it is only within their own jurisdiction that companies can implement equitable pricing policy. Doing so will inevitably lead to a more consistent, transparent and systematic practice of price setting. In particular, companies should further increase their efforts and work with governments and other stakeholders to fight incremental and often substantial price increases by consecutive agents down the distribution channel, before the medicine reaches the end consumer or consumer. This practice undeniably benefits middlemen, but often leads to prices that can no longer be justified to the consumer. While pharmaceutical companies may not always be able, or even legally entitled, to control or intervene, they nonetheless run the serious risk of loss of reputation. Because products are passed through a cascade of distributors, the consumer is likely to hold the manufacturer, and brand name owner, responsible for any perceived or real high end-user prices. In addition, other exogenous factors,

notably protectionism and corruption, may cause ex-factory prices to dramatically and disproportionately inflate. Customs at the border of recipient countries also may levy taxes and tariffs on the importation of medicines.

3.3 Importance of Emerging Markets

While many countries in the world still must develop further to achieve prosperity, it is expected that their income relative to the established economies will gradually converge towards a higher socioeconomic level for many. Given the assumption that the mature 'industrialized' economies will continue to grow as well, albeit at a slower pace, this does not necessarily mean that on a per capita basis the populations of *emerging markets* will overtake those in *established markets* in terms of buying power. Still, it can be argued that that these rising economies should pay their share of global joint costs. In other words, the fixed costs for pharmaceutical R&D should not be amortized on a few high-income countries only, but should be shared by all those which are able to contribute.

The extent to which emerging markets can make a contribution depends on their economic strength and growth expectations. Not capitalizing on emerging markets' economic strength would lead to moral hazard, because these economies would contribute proportionately much less to shared costs (similar to developing countries) than they in fact could bear. The relevant question is thus not whether the emerging markets will keep growing but at what pace and what is the order of magnitude and likelihood for them to join the world economy's *Ivy League*? Prior to the sudden worldwide slowdown caused by the banking crisis and stock market upheaval, the economic growth in emerging markets had already created a sizeable middle class (as shown in the examples below), which – despite significantly lower individual purchasing power than Western counterparts – offers tantalizing sales potential. The McKinsey Global Institute projects India's middle class will grow from 50 to 583 million people in the next two decades; and China's middle class will grow to 612 million by 2025; while Mexico's middle class (families with incomes of between US$7,200 and US$50,000) now accounts for over 30% of Mexican households – or 10 million families. In Indonesia, the middle class is expected to grow to 45 million by 2010. And in Brazil the middle class is now said to represent about 52% of the population, or just under 100 million people (Tickell S., Brenneke M., 2009).

While predictions for the emerging markets remain optimistic, at some point economic growth may start to disappoint. History shows time and again that gaining ground on the prevailing industrial leaders is far easier than overtaking them. This has again been demonstrated most recently in a retrospective study (Eichengreen B., Park D., Shin K., 2011) that examined the economic record of fast growing economies since 1957 – and in particular when they began to slow down. The study's ultimate objective was to identify potential warning signs that could be generalized and would lend themselves to forecasting economic developments. The researchers therefore reviewed countries whose GDP per person on a purchasing-power-parity basis grew by more than 3.5% a year for seven years, and subsequently suffered a sharp slowdown where growth dipped by two percentage points or more. What emerges from the analysis is an estimate of a sort of critical GDP threshold: that is, the growth rate drops from 5.6% a year to 2.1% when per-capita GDP reaches around $16,740 at PPP on average.

Eichengreen and Park (2011) are careful to point out that there is no iron law of economic slowdowns. Nonetheless, looking into the future through this historic lens, China's torrid growth

appears to put it on course to hit the $16,740 GDP-per-head 'threshold' shortly after 2015, well ahead of the likes of Brazil and India. While the implications of such findings are by no means limited to a particular country or countries, they may have special resonance for China for at least three reasons. First, the country accounts for a substantial percentage of the world population. Thus, when China's economy slows, it will have major implications for the welfare of a significant share of humanity. Second, the large and fast-growing Chinese economy is increasingly viewed as a key engine of growth for the world economy. Third, while China recovered faster than expected from the global crisis, its policymakers are grappling with how to sustain growth in the medium and long terms. Hence, China is projected to grow at a rate of initially 6.1 to 7.0 percent per year in the decade 2011-2020, and subsequently at a rate of 5.0 to 6.2 percent in the decade 2021-30. In other words, these findings suggest that China will experience a relative 'slowdown' sometime in the next ten years. This future scenario and prosperity forecast is in-line with projections made in other studies (Hawksworth J., Cookson G., 2008; Maddison A., 2009; Buiter W., Renbari E., 2011).

What are the implications for the differential pricing model as proposed in the previous section? Surely the growth witnessed in emerging economies, especially in countries labelled as BRIC[2] and CIVETS[3] which is demonstrated in table 1, will affect the calculation of differential prices for pharmaceuticals across various countries in the world. Emerging economies' steady economic progress indicates that they are bound to reach a progressively higher income tier at certain milestones during the growth process. This implies that the preferential price 'discounts' currently applied to these countries gradually can return to a lower level that appropriately reflects their economic status. This pattern of world economic progress, and anticipated convergence between various economies, is portrayed in Figure 5. For example, whereas China would be 'entitled' to receive a (theoretical) 'equity' discount at about minus 30% in 2010 based on the country's aggregate GDP level, this would decline to minus 25% in 2015, and minus 19% in 2025, and would eventually become minus 12% in 2050. Table 2 provides an overview of the predicted future trend of economic convergence during the period 2010-2050. Special attention is given here to the increasingly global significance of what are termed 'E7' Emerging Economies: a league on its own comprised of the 'BRIC' economies, plus Mexico, Indonesia and Turkey.

It is important to note that in practice differential pricing decisions are not one-size-fits-all. Product, disease, company, purchaser, ability to pay, country-specific market environment and other variables influence the pricing analysis' outcome. Emerging countries, for example, are immensely complex. They are characterized by extreme cultural and ethnic diversity, marked income inequalities, a significant rural-urban split, with large percentages of the population having very poor access to transportation, infrastructure and other basic services. The complexity is further compounded by rapidly changing and sometimes unpredictable market dynamics. And, of course, each emerging market has its own unique set of trade regulations and industrial policies that influence pricing decisions.

[2] Brazil, Russia, India and China
[3] Colombia, Indonesia, Vietnam, Egypt, Turkey and South Africa

4. Identifying Intra-Country Opportunities for Equitable Pricing

4.1 Health and Wealth Factors

The redistributive effect of differential pricing is not just possible between countries, but also within them for different supply channels and various target groups. Broadly speaking, we define differential pricing between countries as *inter-country* tiered pricing; whereas within the same country it is called *intra-country* tiered pricing. . Considering the heterogeneity of countries and distribution channels, intra-country tiered pricing might not always be feasible or effective. Challenges arise especially when distribution channels for different social segments are insufficiently insulated to minimize the effect of product diversion. This section looks at where intra-country tiered pricing can be best applied. Globally, the countries that may offer opportunities for intra-country differential pricing are the middle HDI countries that collectively represent up to three billion people. We argue that it is best suited to countries in economic transition, such as China, where urbanization has led to a rapidly expanding middle class that enjoys an impressive pace of increasing prosperity, while at the same time poor migrants and rural communities are said to comprise a very vulnerable segment of society.

Applying a large-scale differential pricing policy in a country may represent serious challenges to that government as it requires considerable effort and political will to initiate high-level discussions on welfare and health care system reform. In virtually every country, the debate revolves around the question of redistribution of the financial burden from the poor to the rich through public and private health insurance; although in the case of insurance income is transferred essentially from the healthy to the sick (Balotsky, 2008). Even in affluent countries that can afford extensive social welfare programmes, it appears the debate on health care reform is not over yet. The discussion on whether programmes should be based on equality rather than equity loosely reflects longstanding differences between for instance the American redistribution policy established by government and based on taxation of wealth, versus much of the rest of the world's where societies, such as in Scandinavia, have a tradition of high taxes to finance elaborate social and health programmes. Nevertheless, with regard to access and affordability of medicines for poorer populations, the United States sought to bridge the rich and poor prescription drug divide via the 2003 Medicare Modernization Act. This Act adds prescription drug coverage to the Medicare benefits of retirees, with the objective of alleviating the costs of medication for beneficiaries with low annual incomes or high out-of-pocket medication costs. In a similar attempt, the U.S. pharmaceutical industry teamed up with public and private organizations to create in 2005 the 'Partnership for Prescription Assistance' (PPA) (Havrda et al., 2005).

Stark differences in health insurance coverage and financing exist between high, middle and low income countries. The overwhelming majority of high-income countries have achieved universal coverage for almost all of their citizens; in many instances through mandatory subscription to insurance. Currently, 27 out of the 30 countries of the Organization for Economic Co-operation and Development (OECD) cover all their citizens with health services from pooled funds supplemented with limited direct out-of-pocket payments. Consequently, between 80 and 100% of populations in these OECD countries are formally covered by health insurance and health expenditures covered by government subsidies and private insurance amounts on average to 85% of total expenditure on health (OECD, 2008). This is not the case in lower income countries, where in many instances only

half of the population is covered by formal insurance and only half of the total expenditure on health is covered through third party payments (WHO, 2007; OECD, 2008). Impediments include the unavailability of resources and the inefficient and inequitable use of scarce resources. In countries where the government's share is insufficient or does not exist, private payers cover the cost of needed health services. Of this private expenditure, a significant share is out-of-pocket[4]. Paradoxically, out-of-pocket expenses by households are lowest in high income countries (< 15%) and highest in low income countries (> 50%). Hence, the poor either cannot afford the medicines they need or they buy medicines of poor quality that are very often counterfeit. A secondary effect of the lack of insurance or public sector coverage for medicines is that households have less money for food, housing, education, and other essentials.

4.2 Classifying Country Clusters

The significant out-of-pocket expenses seen predominantly in low- and middle-income countries mean that large numbers of households are not formally covered for the services and medicines they need. It is well documented that this slows down the adoption and appropriate use of medicines. Any attempt at mapping the problem by means of segmentation and clustering of countries should take into account these 'out-of-pocket expenses'. They are one of the key parameters holding back populations from access to medicines. Thus, in the equitable pricing model, 'out-of-pocket expenses' is taken as a proxy measure of how poorly healthcare coverage schemes are implemented. This parameter reflects the ability of the health system to provide access to medicines through the introduction of insurance schemes (either private or public).

For that reason, we introduced the Health Systems Channel Index (HSCI) to the model to emphasize the importance of reducing out-of-pocket expenses – a task for governments and private insurers – as a key strategy toward increasing access to medicines**.** Table 2 illustrates that in most countries the public/private market-share ratio hovers around 60/40% on average. In countries with socialized systems, the public market's share will be even higher. By themselves these percentages do not mean that the poorest populations are covered (although at 95% plus that would be the case). What is misleading in developing countries is that those paying out-of-pocket - mainly because they cannot afford insurance or it is not available - are categorized in official statistics as private market. As a result, the private market as defined in the World Bank's classification system includes people that prefer to receive health care through private channels (paid for by their private insurance company) and those people who have no choice but to pay out of their own pockets, including for medicines. Sadly, the latter group are the poorest who do not profit from risk sharing systems either privately or publicly governed. The HSCI expresses this out-of-pocket health expenditure as a percentage of total health expenditure. The HSCI can thus be calculated by multiplying the private expenditure on health (as a percentage of total health expenditure) with the out-of-pocket health expenditure (reported in statistics as percentage of private expenditure). The formula is presented in Figure 6.

[4] Out-of-pocket expenditure on health care reflects the proportion of expenditure that is not covered by any government subsidy or employer's insurance plan. It includes co-payments, deductibles and payments for over-the-counter medicines, or as is the case in many low- and middle-income countries for medication in general.

Another key variable in the mapping process is the 'level of poverty' found in a country or subpopulations thereof. Amartya Sen, Nobel Prize Laureate in Economics whose work underpins the concept and measures of human development, has argued powerfully for the need to take a multidimensional approach to poverty as well as to human development. Sen's multidimensional perspective has implications for both poverty and deprivation measurement. In accordance with this philosophy, the Poverty and Human Development Initiative at the University of Oxford developed a new set of internationally comparative data (Alkire S., Santos M., 2010). Aided by the improved availability of survey data concerning living conditions for households in developing countries, they have created a new and improved tool, the Multidimensional Poverty Index (MPI), that the United Nations has incorporated into its latest 'Human Development Report' (Human Development Report, October 2010).

The MPI seeks to provide a picture of the prevalence of poverty based on the percentage of households that lack certain basic commodities and services. An additional feature of the novel index is that this approach better identifies long-term trends. For instance, successful reforms in health care usually increase a population's earnings only many years into the future, but with this index impact on earnings quickly reveals itself. An additional strength is that the MPI can be disaggregated by population subgroup within a particular country. Clearly this additional feature is of tremendous practical value for optimizing decision-making in health policy and equity-related pricing. Given the need to accelerate progress towards the health-related Millennium Development Goals (MDGs) and beyond, it is vital to understand the composition of deprivations among different states or provinces, as well as among sub-groups within the same nation, so that interventions may most effectively address people's health and welfare. For more details about its methodology as well as applications for sub-regions and sub-populations, we refer to the above-mentioned articles.

If the MPI is used for differential pricing purposes, it is of particular importance to know that the base for calculating the MPI for a country is the household. Thus, the emphasis is on the individual rather than the country. This base is the calculated product of two components: (1) the headcount or proportion of the population who are MPI-poor (incidence); and (2) the average proportion of weighted indicators in which the MPI-poor persons are deprived (intensity). Figure 6 describes this formula. In fact, the index is a composite of three key dimensions: (1) Health, (2) Education, and (3) Living Standards (e.g. drinking water, sanitation, electricity, flooring, cooking fuel, and assets). These core dimensions are subsequently divided into ten indicators, which we will not discuss in this article. For further information, he Oxford Poverty and Human Development Initiative at Oxford University publishes the range of Multidimensional Poverty Indexes based on data gathered in 104 developing countries (Alkire S., Santos M., 2010).

In summary, our model uses the MPI, in conjunction with the HSCI as described above, as one of the key parameters in identifying intra-country opportunities for differential pricing in developing countries. Graphically, the HSCI is displayed on the horizontal axis (X) in the country identification and prioritization process for differential pricing (as will be described in the next section), whereas the vertical axis (Y) scores the MPI by country. The size of the bubble reflects the size of the population in that respective country. For example, India is situated at the intersection of its MPI (0.296) and HSCI (66.35%) scores. This is illustrated in Figure 7. In the case of India, whereas the MPI score reflects its multidimensional level of poverty level, the relatively high score in HSCI indicates that the number of poor that have to pay for health out-of-pocket is very high. Health insurance

coverage is virtually non-existent so that Indian households have to cover all medical expenses. Under these circumstances, people at the bottom of the pyramid are likely to opt out. Because they cannot afford it, they either do not take or do not finish medication, making the situation worse as drug resistance builds up due to non-compliance.

4.3 Priorities for Differential Pricing

One of the most prominent challenges in designing a sustainable architecture for differential pricing lies in the highly skewed income distribution seen in lower-middle and upper-middle income markets. In countries such as Brazil, India and Thailand, the richest 10% of the population owns more than 30% of the wealth and their per capita income is comparable to those living in high income countries. The bottom 10-20% in these countries, however, is often poorer than the average per capita income in least developed countries [World Bank, 2009]. Because most people in these poorer market segments pay for medicines out-of-pocket, price sensitivity is acute.

According to Yadav (2010), intra-country tiered pricing can be implemented only when the high income and low income markets in the country obtain the medicines from different channels, assuming that the channels are perfectly sealed. That is, no product can flow from one distribution channel to another and customers in one market cannot purchase the product in the other market. In developing economies, the degree of separation between the physical product distribution channel through which the poorest income quintiles seek treatment and the distributional channel through which the richer segments seek treatment provide an opportunity for intra-country differential pricing that may not be available in industrialized contexts (although Medicare and Medicaid are exceptions to the rule). Generally, developing countries and emerging economies have two health provisioning channels: publicly financed government delivery systems and privately financed (mainly out of pocket) market systems. This provides a natural wedge which can be leveraged to charge different prices in different channels and to reach specific segments of the population at price points which they can truly afford. Another natural wedge that can be leveraged through intra-country differential pricing in developing countries is the urban-rural income divide**.**

Figure 7 illustrates that by using market segmentation parameters like MPI (multidimensional poverty) and HSCI (out-of-pocket health expenditure), countries can be grouped into four clusters, each posing challenges but predominantly offering major opportunities for practicing intra-country tiered pricing. As will be explained below, it is no coincidence that countries in economic transition offer the greatest opportunity. Whereas the poorest countries (cluster 1) invariably require low prices (presenting limited room for differential pricing within the country itself), the richest segment (cluster 4) predominantly represents citizens that are relatively affluent and covered by either private or public insurance. By starting in cluster 1 (scoring high on the MPI), and going clockwise to respectively cluster 2 (scoring high on both MPI and HSCI), 3 (scoring less high on MPI, but high on HSCI) and 4 (scoring less high on both MPI and HSCI), one follows in a way a pattern of socioeconomic development. Consequently, the highest opportunity for differential pricing is in the middle clusters (with heterogeneous populations) and not at the extremes (representing clusters with homogenous populations of which the majority of citizens is either predominantly rich or poor).

Cluster 1

Cluster1 is comprised of low-income countries with high rates of poverty and underdeveloped public health systems. The majority of these countries are in Africa and receive donor funding for health services capacity building and procurement and distribution of medicines. As a result, their score on the HSCI is rather good in that they appear to bear a limited out-of-pocket expense burden, but the score does not reflect that. In the long run local governments must invest in health.

Achieving better health outcomes for this cluster of countries, which includes millions of people who live on less than US$2 a day, is a prominent priority on international development agendas. Governmental and private donors are working in collaboration with supranational agencies, such as the WHO and centralized procurement agencies, to negotiate low, subsidized prices for pharmaceuticals on behalf of least developing countries. In this way, suppliers obtain guarantees on volumes while risks are hedged via pooling and donor guarantees of funding. Additionally, new public private partnerships, such as The Global Fund to Fight AIDS, Tuberculosis, and Malaria (GFATM) and The Global Alliance for Vaccines and Immunization (GAVI), have arisen, focusing exclusively on international health and including improved access to medicines in their mandate. This heightened quest for more effective ways to accelerate progress also has spawned interest in exploring innovative financing mechanisms for health services and products. Examples of such initiatives include the International Finance Facility for Immunization (IFF-Im), the Airline Solidarity Contribution (ASC, or simply, 'the airline tax'), and the Advanced Market Commitment (AMC) (de Ferranti D., Griffin C., Escobar M., Glassman A., Lagomarsino G., 2008). Thus, for the foreseeable future, external funding and technical assistance from more affluent industrialized countries and private philanthropic donors to countries in Cluster 1 is likely to continue.

Cluster 2

Cluster2 is comprised of lower-middle income countries where over 50% of total health expenditures are paid for out-of-pocket and due to lack of health insurance are absorbed by private household budgets. The gap between haves and have not's is greatest in the countries in this cluster. It includes India, which although it resembles in some ways countries in Cluster 1, uniquely combines elements of extreme poverty and wealth. Moreover, expenditures on health differ by a factor of seven between the major states. For example, public expenditure per person in 2004-05 was estimated to be INR93 in Bihat compared with INR630 in Himachal Pradesh (Government of India, 2009). India's health outcomes have improved with time, but they continue to be strongly determined by factors such as gender, caste, wealth, education, and geography (Balarajan Y., Selvaraj S., Subramanian S., 2011).

Cluster 3

Cluster 3 consists of lower-middle income countries with significant populations (including China, Philippines, Vietnam, and Egypt) that score significantly better on the multidimensional household poverty index, but whose ratio of out-of-pocket expenditures is comparable to countries in Cluster 2. China is widely acclaimed as a miracle economy, yet over the recent period of rapid economic growth the country's reputation for health care has been slipping (Tang S., Meng Q., Bekedam H., Evans T., Whitehead M., 2008). Before the economic reform launched in 1978, over 90% of the rural population in China was covered by the Cooperative Medical Scheme, while the Government

Insurance Scheme and Labour Insurance Scheme provided almost free health care to the employees of government agencies and public institutions in Chinese cities. Economic reform has brought profound changes and the Cooperative Medical Scheme now has collapsed in most rural areas. Today there is a large divide between urban and rural areas. .

To bridge the health care gap, the Chinese government has pledged to accelerate its investment in modernisation of the public-health system, including disease prevention and health promotion, and to establish three health-insurance schemes: 1) rural cooperative, ; 2) urban employee and resident basic health-insurance, ; and medical financial-assistance for poor people. While the aim is to ensure better access to essential health care, China still has much to do to move toward universal access and covering the cost of medicines. China provides, therefore, an important example of a country where utilizing the urban-rural divide in income levels can be used to create a price differential scheme for pharmaceuticals.

Cluster 4

Cluster 4 is comprised primarily of middle-income countries that are on the right track economically and in terms of health care provision. Although every country is unique, the experiences of arduous reform in Colombia, Mexico, and Thailand are illuminating because of the changes that they undertook and the problems they had to resolve along the way (Hughes D. et al., 2007; Gakidou E. et al., 2006; Uribe A., 2006; Scott J., 2006). While subsidising insurance for citizens required a substantial injection of public resources by the government in these countries, access to and use of health services has improved because the insured are more likely than the uninsured to seek care when needed. All of these countries have persisted with health care reforms and succeeded in increasing coverage significantly, while reallocating public resources to reduce disparities across population groups. For example, 83% of Colombia's population is insured and 95% of Thailand's. In Mexico, an additional 11 million people, most of whom low-income, have been insured under the Seguro Popular programme. And in Brazil, the Federal Constitution which states that health is a human right drives government's engagement by; thus it is the state's responsibility to deliver health care nationally and free of charge (Article 196). In 1990, these constitutional provisions led to the creation of the Sistema Universal da Saúde (SUS). Brazil's public health system now covers 190 million people (although much remains to be done in poor areas, e.g. favelas). It is considered to be the largest in the world). Furthermore, Brazil's programmes are informed by the concept that health activities can serve as an engine of domestic industrial development (Guennif S., Ramani S., 2010).

Finally, industrialized countries with highly developed health care systems like Japan, Europe, the United States, Canada, and Australia are not represented in the MPI, which concentrates instead on low- and middle-income countries. Undeniably, pockets of poverty exist in these countries and so the highly-industrialized countries would graphically be positioned in the lower left-hand corner of the graph.

5. Creating a Sustainable Environment and Enabling Policies

5.1 Parallel Importation

The avoidance of reverse flows of imports is the thorny issue in designing differential pricing systems. It is evident that to maintain price differentials barriers must exist to the reverse flow of products from low-income to high-income markets, or between market segments within the same country. Reportedly, the industry and its investors are wary of experiments – at least visible ones - with different pricing models in emerging markets because of the potential effect of eroding margins in mature markets. Parallel trade flows remain a major concern to industry, which wishes to protect its higher price markets against price erosion through arbitrage (S. Tickell, M. Brenneke, 2009; Barton, 2001).

Arbitrage is the practice of taking advantage of differences in the cost of production between geographically defined markets. The justification is that the benefits ultimately accrue to the consumer. But this is hardly the case with pharmaceuticals that are re-imported either in the country of origin, or in any other country with relatively higher prices (and this despite the fact that they are often re-packaged by the arbitrator). Re-importation of the same product is essentially another way to import concessionary prices, or price controls, from other countries without explicitly adopting them in the imported country. As such, the economic consequences of parallel trade or re-importation are roughly the same as directly imposed price controls. However, under a regime of national exhaustion of intellectual property (IP) rights, an IP owner could prevent parallel import of his product from another country where it is sold by him or by an exclusive distributor. By contrast, under a regime of international or regional exhaustion, the IP owner would lose his exclusive right once the product is launched in any particular market for the first time. In general, countries are free to determine their preferred exhaustion regime. In other words, countries can freely decide on whether to permit or ban parallel trade. The only provision in the multilateral WTO agreements that explicitly deals with the treatment of parallel trade is Article 6 of the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS). The matter has been complicated by the European Court of Justice (ECJ) rulings in various cases that the free circulation of goods within the common market takes precedence over the protection of IP, and that therefore parallel trade within the common market is legal. That is, exhaustion applies upon first sale anywhere in the EU region.

It could be argued that regulators in a regional market like the EU take an overly optimistic approach in using rules about competition to protect parallel trade when such a rigid approach is not warranted in the case of nationally price-controlled pharmaceuticals. Fortunately, IP exhaustion within the EU region has its limitations (Rey P., Venit J. 2004). Firstly, exhaustion does not extend to countries outside the common market. Secondly, with regard to potential restrictions for parallel trade within this common market, the pertinent question is whether supply quotas for foreign wholesalers imposed by the original manufacturer are illegal. The European Court of Justice (ECJ) concluded in *Bundesverband der Arzneimittel-Imprteure and Commission of the European Communities vs. Bayer* that unilateral supply quota systems are not necessarily prohibited, as long as they do not constitute a contractual agreement prohibiting parallel trade. In other words, unilateral restraints on sales from an original manufacturer to foreign wholesalers are not necessarily illegal under Article 81 of the EC Treaty. Any contractual agreement explicitly prohibiting parallel trade

within the common market would be void, however, under this law. The ruling leaves room for containing the damaging effects of parallel trade.

5.2 Reference Pricing

International reference pricing refers to the virtual component of parallel trade, or re-importation, as described earlier. Given the wide range of countries that practice this type of pharmaceutical price control, the impact of external price referencing is likely to be much greater in negatively affecting revenue compared to physical parallel trade. Establishing pharmaceutical reimbursement in a country based on a basket of external reference prices, usually deducted from an arbitrary selected sample of countries with different wealth, the majority of which charge significantly lower prices, leads to a system that in principle would defeat any benefit offered by differential pricing on a global scale. That is, the practices of international price referencing versus differential pricing are not compatible. Additionally, the quest by some to openly publish worldwide prices through a global database is counterproductive. Despite all good intentions, customers naturally will gravitate toward the lowest price level, leading to an untenable situation in price differentiation that would essentially favour those who cannot afford standard prices. It would be better to not publish the various trade discounts granted to poorer nations, consumers, or large purchase groups.

5.3 Buyer Monopsony

Governments may establish price controls and are in many instances the single payer for health care services. This leads to imperfect competition, thus allowing the monopsonists buyer to dictate the terms to its suppliers. This may drive prices down, leaving little or no room to the supplier for recouping R&D investments. While this may be beneficial to consumers in the short term, all too often monopsonist markets lead to distortions and threaten the long-term security of supply, especially if the focus is exclusively on low prices.

It has been argued that a very large pooled procurement scheme might actually exert excessive downward pressure on prices, rendering the market so unattractive that some suppliers would withdraw (Jarrett, 2003). More specifically, Leach B., et al. (2005) report that 'this risk probably arises (only) in the case of a very large and powerful joint procurement agency with global outreach'. If prices are unreasonably low, scenarios are conceivable without any doubt for companies to evaluate withdrawal from markets that supply poor countries. In theory, the larger multinationals may be in a position to afford losses on such transactions (at least temporarily and up to a certain extent), but for the majority of small and mid-sized pharmaceutical and health technology companies this is not an option. Nor is it one for emerging market manufacturers in the foreseeable future.

Pooled procurement, another approach to public procurement, which has been adopted in various parts of the world in recent years, is an arrangement by which a number of countries jointly entrust their pharmaceutical purchasing to a single body, generally working at the regional level. Essentially, a regional pool assumes the responsibility for provision of all medicines for its member states, either across the board or within a defined therapeutic area. The pool remains dependent on the individual member states for forecasts of need, so that ordering is adjusted to real requirements. From an economic viewpoint, if the region is homogenous, this could be an effective mechanism as the prices paid in wealthier segments compensate for the prices paid in the poorer ones. But if the pool

includes mixed economies, prices may rise beyond the level the poorer economies in the segment would otherwise have paid given their income level.

5.4 Intellectual Property

We believe that the concept of patents is basically good. An inventor is granted exclusive rights by a state that include a monopoly for a limited period of time (defined by WTO at a minimum of 20 years) in return for disclosing the details of the innovation in the public domain. Publicly sharing advanced technologies, rather than keeping them private, further spurs innovation. More importantly, patents represent an incentive for efficient research and development. On the downside, since a patent is, in effect, a limited property right, it does provide the right to the inventor to exclude others from making, using, selling, or importing the innovation for the term of the patent. In the research based pharmaceutical industry, patent applications are filed before the regulatory process is actually complete, effectively reducing the period of patent protection by nearly 50% (Grabowski, Vernon, 1996). During this term the compound faces competition from existing and new compounds. At the expiration of the patent term, generics will enter the market.

Controversy has arisen around the question of whether the patent strikes a balance between the interest of the patent owner and what are seen by some critics to be overriding public health concerns. This trade-off, however, is built into the pharmaceutical patent system. The current system requires significant disclosure of information, which leads to the creation of new pathways for improved or brand-new medicines that subsequently compete with each other, driving prices down. Through this quid-pro-quo agreement between society and the inventor, key information about the invention is made available to other researchers, adding to the world's body of knowledge. Without the patent system, this knowledge would remain unavailable, or even secret. Hence, because of the patent system, product innovators or health researchers do not have to reinvent the wheel. TRIPS has been largely successful in providing a forum for nations to agree on an aligned set of patent laws. Conformity with the TRIPS agreement is a requirement of admission to the World Trade Organization (WTO), evidence many nations believe is important. This has also led to many developing nations enforcing patents laws in line with global practice, in contrast to historical practice where they may have developed different laws to aid their development.

In summary, the principle of differential pricing does not stand in the way of intellectual property rights, and *vice versa.* As outlined in previous sections, differential pricing can be widely used and can inform the discussion about how to make medicines more affordable. In addition, preserving intellectual property rights is the linchpin of achieving not only short term (static) efficiency but also long term (dynamic) efficiency, structurally paving the way for sustainable access to medicines. Contrary to popular belief, patents do not represent the major hurdle to worldwide access to medicines. Of the 325 medicines on the WHO's Essential Medicines List, over 95% are off patent, and yet one-third of the world's population has no reliable access to these medicines (Attaran A., 2004). Strengthening health care infrastructure, educating and training professional staff and financing programmes by making health a priority are areas that deserve greater attention instead.

5.5 Neglected Diseases

By definition, a differential pricing policy cannot be applied to medicines for diseases that are predominantly, or sometimes exclusively, prevalent in lower income countries. These diseases,

which are also called neglected diseases, are primarily tropical diseases such as malaria, tuberculosis, dengue fever, visceral leishmaniasis, sleeping sickness, and Chagas disease. With regard to availability of pharmaceuticals, a distinction should be made between *international neglected diseases* and what are called *orphan diseases* such as cystic fibrosis which mainly affects patients in developed markets. What both categories have in common is the risk to be deprioritised in drug development because of the lack of economic incentives for the innovator or manufacturer. Both undeniably represent an undisputable medical need: the first because of the epidemic proportions in poverty stricken countries and the other purely because of its life threatening nature at the patient level.

Kettler suggests that the main factor in underinvestment in pharmaceutical R&D for neglected diseases is the estimated low size of market (Kettler, H., 2000). Under these circumstances pharmaceutical companies judge that the return on investment in R&D for neglected diseases that are prevalent in poor countries will be less than the return on an equivalent investment in medicines for the developed world. The phenomenon is generally known as *market failure* and justifies the mediation of government subsidies to help remedy the problem. Kremer M. and Glennerster M. (2004) argue that society actually benefits from such interventions. The social returns on investment in malaria vaccine innovation, for example, are likely to be at least ten times higher than the economic returns. It also has been argued that the emerging pharmaceutical industry in developing countries such as India, Brazil, Thailand or Argentina will invest in R&D for medicines for internationally neglected diseases if these countries require stronger patent protection (Kettler H., 2002; Kettler H., Modi R. (2001). Meanwhile, innovative international public-private partnerships -- the Malaria Medicines Venture (MMV), the Malaria Vaccines Initiative (MVI), The TB Alliance (for the development of drugs), AERAS (for TB vaccines), IAVI (for Aids vaccines), and others -- are exploring, accelerating, and funding R&D opportunities in neglected infectious diseases.

Push and pull mechanisms can effectively stimulate R&D of medicines for neglected diseases. The expectation is that external financial interventions will help mitigate the problem of lack of access to affordable medicines in developing countries. On the supply side, technology *push* mechanisms are considered to work best in the early phases of innovation done by publicly funded research institutions (e.g. NIH), as well as by tax credits to stimulate R&D programmes conducted by the private sector. *Pull* programmes include market replacing incentive programmes such as advance purchase or advance market commitments (e.g. AMC), the funding of which is backed mainly by OECD governments, philanthropists, or innovative financing mechanisms like the International Finance Facility (IFF). Other incentive mechanisms such as Medical Prize Awards, Patent Buyouts, Patent Pools, and Open Source Innovation require further investigation before they can be implemented (Daems, 2008).

6. Conclusions

The focus of this article has been on examining the public policy and corporate strategy aspects of differential pricing. Estimating the clinical, social and economic value a product has in the consumers' or buyers' view is fundamental to price setting, but it is just one facet of the role of price in commercial decision-making and profit optimization. Pharmaceutical prices are further determined by competition and the respective market powers of the parties involved who, as a whole, operate within the boundaries of international conventions and law, covering trade, competition, and in the case of access to medicines, human rights.

We conclude that a system of global differential pricing would predominantly benefit countries with transitional economies, including those labelled conventionally as low-income, lower-middle and upper-middle income. The degree to which the proposed conceptual framework and associated analytical model offers a sustainable solution to the access, affordability and pricing of pharmaceuticals depends on: 1) the economic development status of a country, 2) the value of particular medicine in its therapeutic class, 3) the incidence of disease and 4) the extent to which market segmentation can be applied in practice. The authors further highlight the political commitment that is needed to make equitable, differential pricing work for all stakeholders. We have made a number of suggestions about how to remove the main barriers or mitigate their impact, and on how to create an enabling environment. The key findings are summarized as follows:

All sectors in society must work together to ensure access to medicines and at the same time advance innovation:

- Governments in each and every country are ultimately responsible for securing the health of their citizens. They must ensure appropriate domestic health financing, the strengthening of the health care infrastructure and sound regulation of pharmaceuticals along the entire discovery and supply chain.
- The role of industry in developing, manufacturing and delivering medicines is critical in the effort to achieve global health targets. Equally important is its responsibility in determining the right pricing policy, as pricing remains the cornerstone of a competitive market. The challenge will be to implement differential pricing in conjunction with value-based pricing for a wider basket of medicines.
- Supranational agencies and philanthropic donors play an important role in financing the supply of drugs, vaccines, and medical diagnostics to poverty-stricken areas. The research-based pharmaceutical industry's responsibility is to help address diseases that affect poor nations in particular.

An integrated differential pricing framework comprises social, economic and health system variables:

- Inter-country differential pricing consists of defining price tiers on the basis of calculation of equitable discounts. The logarithmic function of the gross national income adjusted for purchasing power parity, or the human development index by country, could serve as proxy measures for ability-to-pay.

- Intra-country differential pricing triggers a redistributive effect within a geographic entity (i.e. nation or region). Equitable pricing based on intra-country market segmentation can be applied to different target groups; i.e. to different supply channels and to geographically divided rural and city consumers.
- Differential pricing within, as well as between countries, would significantly increase affordability for poor populations in countries with a skewed income distribution and no or limited health insurance coverage. These populations can be mapped using household welfare and health systems indicators.

Implementing differential pricing requires creating a supportive environment and enabling public policy:

- Political support for tiered pricing – Politicians, governments, trade regulators and the judiciary should publicly acknowledge that *economic price discrimination* produces positive effects that enable firms to service nations, regions and population groups who would otherwise not be able to afford the purchase of effective medicines.
- Parallel trade and counterfeiting – Governments and legislators should take the necessary precautions to avoid parallel trade and counterfeiting of brand name medicines. The ability to practice differential pricing depends on the absence of arbitrage between market segments. Prices and rebates to buyers should not be made public because this leads to price referencing, defeating the purpose of differentiated pricing.
- Intellectual property rights – Stakeholders should acknowledge that intellectual property represents an asset for the firm because it influences its ability to innovate and practice differential pricing. The benefit to stakeholders is that private and public markets can be entered simultaneously as of the date a compound is launched.
- Funding of neglected diseases – All parties should realize that differential pricing has its limits, and cannot by itself solve the problem of affordability of medicines for neglected diseases that disproportionately affect developing countries. Special incentive mechanisms must be designed and applied to support R&D in this field.

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Figure 1 : Differential Pricing and Equitable Pricing : Mirror Concepts

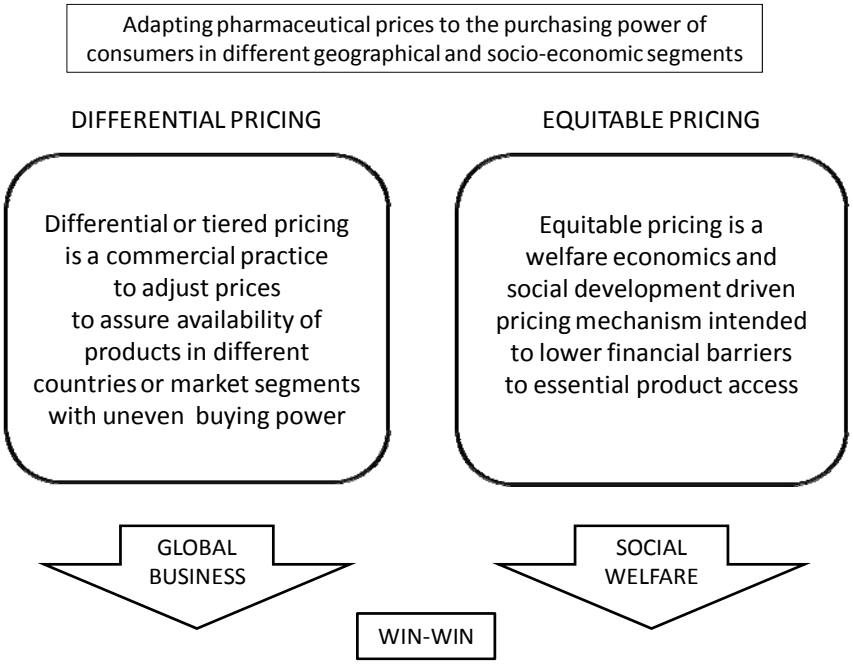


Figure 2 : Reconciling Market Access and Pharmaceutical Innovation

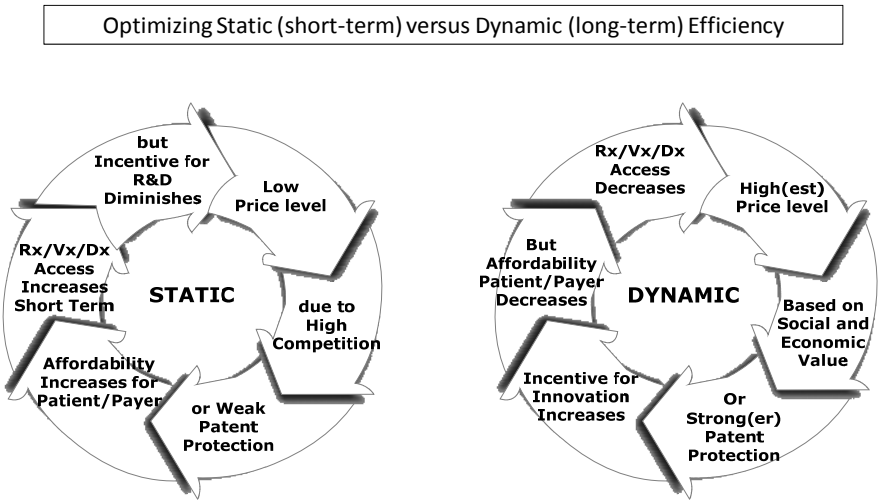


Figure 3 : Equity Curve based on National Income adjusted for Human Development Index (HDI)

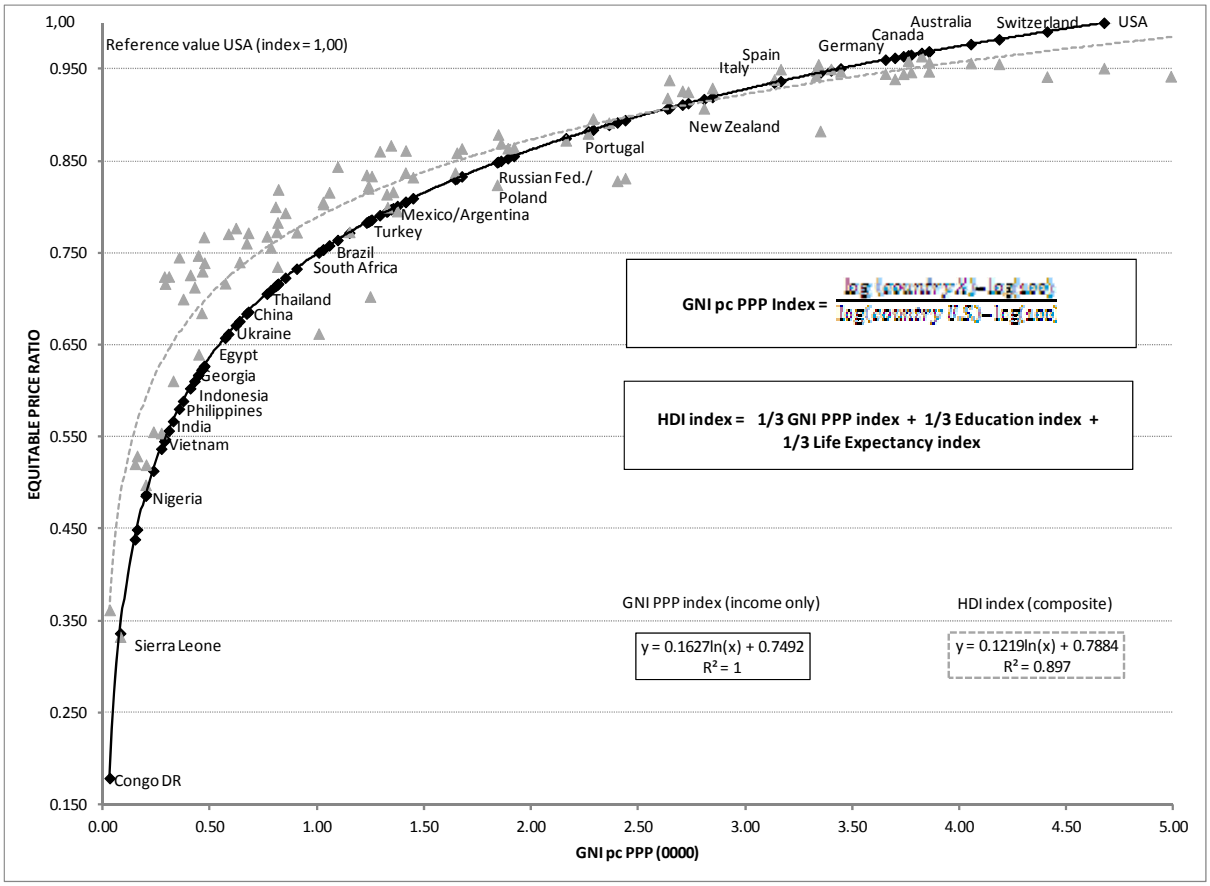


Figure 4 : Benchmarking Real Prices versus Equitable Price Index

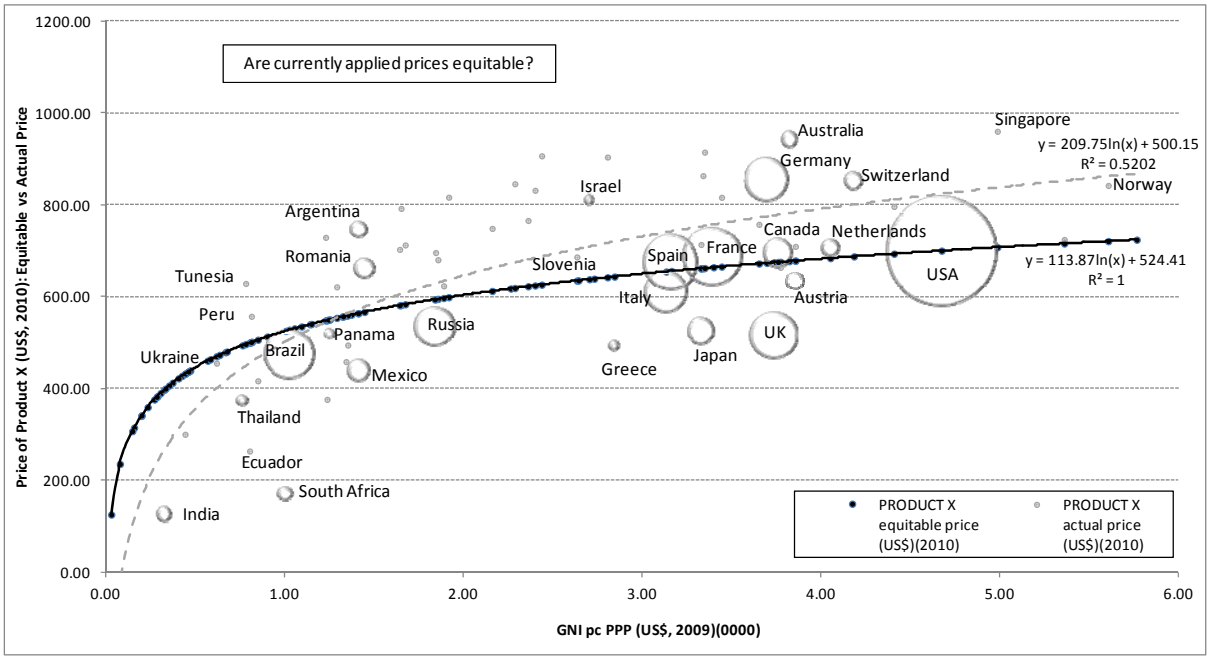


Figure 5 : Trend of Equitable Discounting in Period 2010-2050

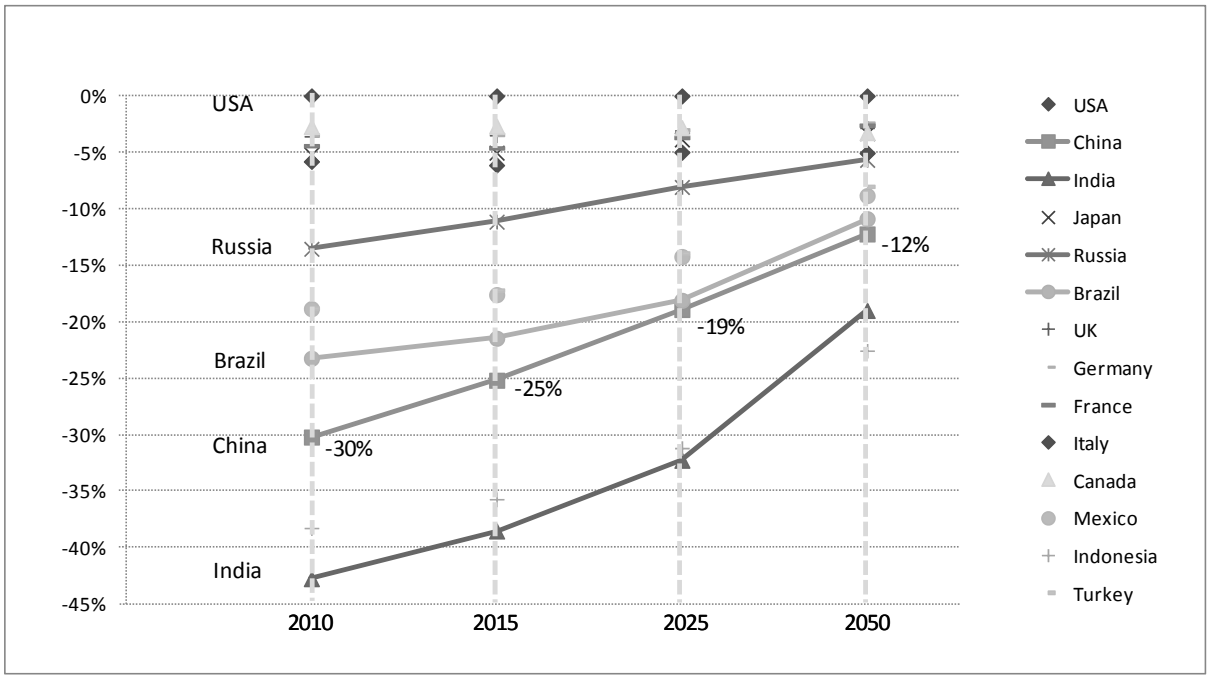
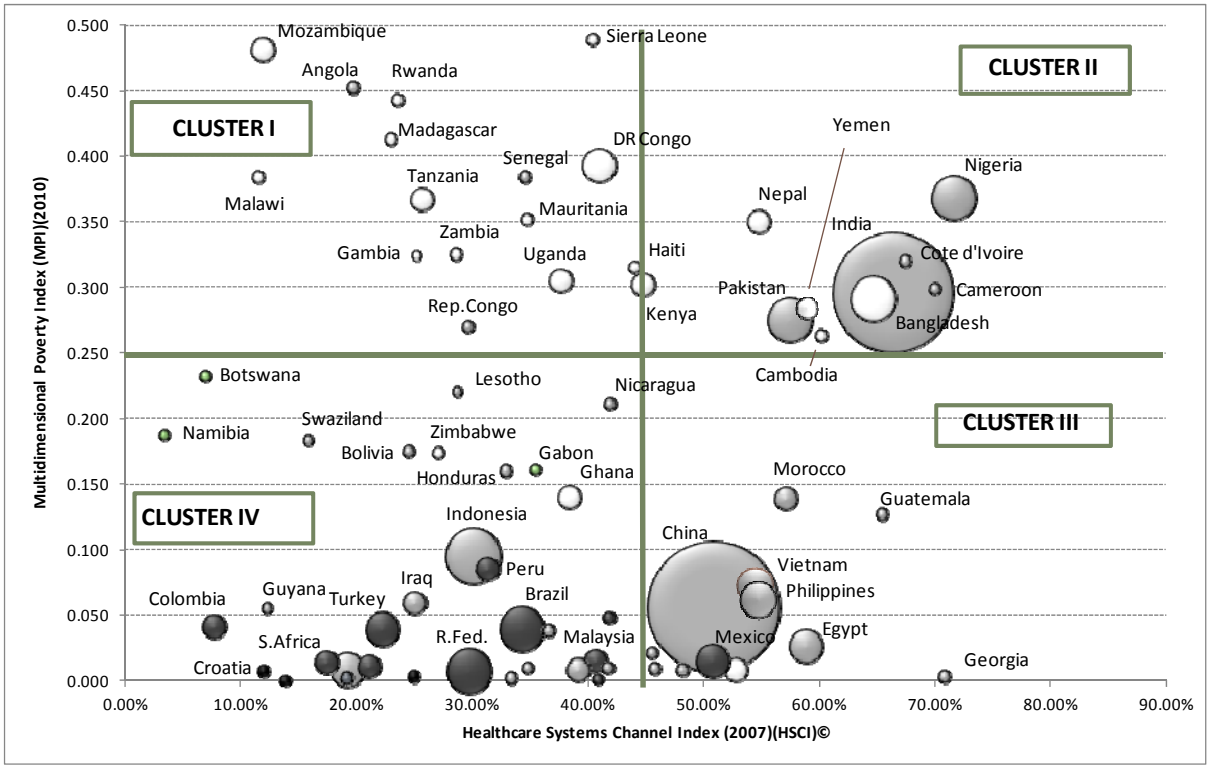


Figure 6 : Two-Dimensional Mapping based on MPI and HSCI

THE MULTIDEMENSIONAL POVERTY INDEX (MPI)	THE HEALTHCARE SYSTEMS CHANNEL INDEX (HSCI)
Enables identification of concomitant deprivation within households, and the clustering of deprivations in different countries.	Out-of-pocket health care expenditure as % of total health expenditure. Measure of how poorly health systems are developed.
MPI = A x H H= Headcount or proportion of the population who are poor (incidence) A = Average proportion of weighted indications (health, sanitation, education) in which households are deprived (intensity)	HSCI = P x O P= Private expenditure (as % of total health care expenditure) O = Out-of-pocket health care expenditure (as % of private expenditure)

Figure 7 : Two-Dimensional Mapping (focus on low and middle income countries)



Legend: High income Upper-middle income Lower-middle income Low income

Table 1 : Growth Projections of GDP per capita for Selection of Countries (2010-2050)

Country	GDP pc PPP (US$, 2010)	GDP pc PPP (US$, 2015)	GDP pc PPP (US$, 2025)	GDP pc PPP (US$, 2050)	GDP pc PPP Growth Factor
US	46,138.49	50,505.49	58,569.23	94,225.98	x2
China	7,226.35	10,529.75	17,549.04	40,778.19	x6
India	3,348.97	4,587.32	7,490.61	25,637.43	x8
Japan	33,565.38	36,936.96	45,825.72	75,166.93	x2
Russia	20,102.04	25,249.63	35,029.51	63,933.25	x3
Brazil	11,091.55	13,276.33	18,476.30	44,718.56	x4
UK	37,043.24	40,654.01	48,167.81	77,613.51	x2
Germany	37,279.59	40,833.59	48,375.47	79,841.96	x2
France	35,197.70	37,907.89	46,316.91	78,901.87	x2
Italy	32,325.76	34,487.74	42,620.01	66,691.37	x2
Canada	39,061.92	42,743.94	48,954.74	75,384.89	x2
Mexico	14,518.83	16,885.98	23,662.02	51,470.14	x4
Indonesia	4,408.17	5,463.52	8,022.20	20,088.95	x5
Turkey	14,565.64	17,309.48	24,143.05	54,453.39	x4

Source: Adapted from PwC economic data (2011); United Nations population data (2008)

Table 2 : Gradually Decreasing Discount Rates by Country (2010-2050)

Country	% Discount 2010	% Discount 2015	% Discount 2025	% Discount 2050	Range of % discount 2010-2050
USA	Benchmark	Benchmark	Benchmark	Benchmark	
China	-30	-25	-19	-12	-30 to -12
India	-43	-39	-32	-19	-43 to -19
Japan	-5	-5	-4	-3	-5 to -3
Russia	-14	-11	-8	-6	-14 to -6
Brazil	-23	-21	-18	-11	-23 to -11
UK	-4	-3	-3	-3	-4 to -3
Germany	-3	-3	-3	-2	-3 to -2
France	-4	-5	-4	-3	-4 to -3
Italy	-6	-6	-5	-5	-6 to -5
Canada	-3	-3	-3	-3	-3 to -3
Mexico	-19	-18	-14	-9	-19 to -9
Indonesia	-38	-36	-31	-23	-38 to -23
Turkey	-19	-17	-14	-8	-19 to -8

Source: Adapted from PwC economic data (2011); United Nations population data (2008)

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