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### Publication status and date:

Published: 10/01/2014

### Document Version

Publisher's PDF, also known as Version of record

### Citation for the published version (APA):

Niëns, LM. (2014). *Affordability in Health Care: Operationalizatoins and applications in different contexts*. [Doctoral Thesis, Erasmus University Rotterdam]. Erasmus Universiteit Rotterdam (EUR).

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# Affordability in **Health Care**

Operationalizations and Applications  
in Different Contexts

*Laurens M. Niëns*





# **Affordability in Health Care:**

Operationalizations and Applications in Different Contexts

Laurens M. Niëns



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**Affordability in Health Care:**  
Operationalizations and Applications in Different Contexts

**Betaalbaarheid in de gezondheidszorg**  
operationalisaties en toepassingen in verschillende contexten

**Proefschrift**

ter verkrijging van de graad van doctor aan de  
Erasmus Universiteit Rotterdam  
op gezag van de  
rector magnificus

Prof.dr. H.A.P. Pols

en volgens besluit van het College voor Promoties.  
De openbare verdediging zal plaatsvinden op

vrijdag 10 januari 2014 om 13:30 uur

door

**Laurens Mathieu Niëns**  
geboren te Weert



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### **Overige leden:**

Prof.dr. E.K.A. van Doorslaer

Prof.dr. J.J. Polder

Prof.dr. C.A. Uyl-de Groot

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# Chapter 1

Introduction





## 1.1 BACKGROUND

Over the last decades, total health expenditures have increased significantly (Meltzer, 2001; Folland et al., 2004). Governments in low- and middle-income countries (LMICs) as well as in high-income countries face the difficult challenge of ensuring that necessary interventions are accessible for those who need them, while keeping care affordable. Since good quality health care and new medical interventions can be expensive, the process of balancing the goals of ensuring access to good quality health care for all citizens and ensuring affordability of health care is a difficult one (Weale, 1998). The need for both efficient financing and budget allocation in health care hence is ever increasing. Economic resources being limited, the issue of how health care can be organized in an affordable manner is at the heart of many policy discussions. It is ultimately also scarcity that forces politicians and policymakers alike to decide on how to organize health care, what interventions to implement and how to finance them. This is a daunting task since setting priorities or rationing care which encompasses “explicit and regular attempts to define how much of which services should be provided and moving resources between services” (Hunter, 1997), clearly are unpopular topics among constituents.

Although both LMICs and high-income countries are confronted with issues of scarcity and affordability, the degree of scarcity obviously differs between these countries. For many people in LMICs the right to health, as laid down in several treaties (United Nations General Assembly, 1948; United Nations Office of the High Commissioner for Human Rights, 1966), is still not secured (Backman et al., 2008). As the majority of LMICs do not have a properly functioning system of health care financing through health insurance, out-of-pocket payments (OOP) still account for a large proportion of all health care expenditures (McIntyre et al., 2006; Van Doorslaer et al., 2006; Lagarde & Palmer, 2011). Hence, besides questions about which care interventions to invest in, ensuring that their populations can financially and physically access the services they need in either the public or private sector is an important challenge LMICs face. Especially when OOP payments are the main source of health care financing, at the patient or micro level, access to health care may be strongly influenced by *affordability* or *ability to pay* (Bruce & Grana, 1998).<sup>1</sup> Therefore, for LMICs, improving the level and distribution of public health and establishing appropriately functioning health care

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1. Other parameters influencing access are: the availability of services, the distance between health care facilities and patients, the appropriate organization of these facilities (decent opening hours, appointment systems etc.) and the acceptability of providers' attitudes towards patients (Penchansky & Thomas, 1981).

systems, is vital. Next to being an important goal in its own right, perhaps as the single most important capital good, a healthy population is also an essential prerequisite for development. This is highlighted by the eight Millennium Development Goals, three of which are directly related to health (United Nations Development Program, 2012b).<sup>2</sup> While the disease burden in LMICs was mostly caused by communicable diseases in the past decades, more recently the burden of non-communicable (or lifestyle) illnesses in these countries is rapidly increasing (Lopez et al., 2006). This epidemiological transition, next to the fact that populations in most LMICs are growing, raises additional questions about an optimal provision of health care in the context of clear budget restrictions at the macro and micro level. Consequently, governments in LMICs need to set priorities and ration health care services. With funds being (much) scarcer than in developed countries and health care systems mostly being underdeveloped (Leatherman et al., 2010), presumably, for these countries deciding in which care to invest is more urgent and may have larger health consequences.

High-income countries also face problems regarding the affordability of health care. However, in most high-income countries (social) health insurance systems are functioning and *accessibility* is not as strongly linked to *ability to pay* as in many LMICs. Indeed, in those health insurance systems, solidarity between high and low risk groups and high- and low-income groups is ensured through the pooling of risks and pre-paid contributions. This leads to accessible health care for the (vast) majority of citizens and patients in high-income countries (Thomson et al., 2009). The problem that many of these countries face is that of rising health care expenditures, raising questions regarding the sustainability and affordability of (social) health insurance systems. Aging populations, being ahead in the epidemiological transition to non-communicable diseases compared to LMICs and expensive new technological innovations are an important cause for this (Newhouse, 1992; Costa Font & Sato, 2012). Thus, high-income countries are confronted with difficult decisions regarding how to maintain an affordable health care system at a macro-level. More private payments and limiting the entitlements of the insured are two ways of doing so, but both may lead to issues of affordability of care at a micro-level.

The above briefly introduces the topic of this thesis; the issue of affordability in the health care sector. The main aim of this thesis is to contribute to the understanding of the role and importance of affordability in relation to choices in health care and to its measurement. This thesis does so through several studies in both LMICs and high-income countries.

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2. Reduce child mortality, Improve Maternal Health and Combat HIV/AIDS, Malaria and other diseases.

## 1.2 RESEARCH QUESTIONS

The main research questions of this thesis are the following:

**1. How can the affordability of health care services be measured in LMICs?**

This thesis addresses this question in part I, in which chapters 2 – 4 focus on affordability at the micro level in LMICs.

**2. How can the concept of affordability inform choices regarding the benefit package of a mandatory health insurance system?**

With a focus on a high-income country, this question is addressed in part II, chapter 5.

**3. How can choices regarding the allocation of scarce resources be informed?**

In part III of this thesis, chapters 6 – 8 indicate how policymakers can be provided with information to inform choices in the areas of breast cancer and HIV/AIDS.

## 1.3 HEALTH ECONOMICS AND AFFORDABILITY

Health economists try to inform policymakers on how to best use their (limited) resources. To see what the impact of health care expenditures is on family incomes and poverty, and hence study the issue of affordability, health economists have developed and worked with the impoverishment and catastrophic payment methods (Wagstaff & Van Doorslaer, 2001; Wagstaff & Van Doorslaer, 2003). The catastrophic payment method calculates the proportion of the population that would spend more than a certain percentage of their income to pay for some health care commodity. Hence, it expresses affordability in terms of a maximum percentage of income to be spent on a certain good. Beyond that percentage the payment for the commodity is deemed “catastrophic” (unaffordable). The impoverishment method estimates the proportion of the population that would be pushed below some relevant poverty line by procuring a given medicine. Hence, this method focuses on the residual income after a purchase and works from the premise that people should not fall below some absolute minimum level of income due to a purchase. If people do or would, the good can be considered unaffordable. Applying these methods requires information on the price of a commodity, incomes and some level of unacceptable burden, i.e., the maximum percentage of income to be spent on some good or the minimum income level left after a purchase. However, in many LMICs the micro data that are commonly used to operationalize these methods are not readily available, limiting their use and hence the monitoring of affordability. Furthermore, the impact of the thresholds used -i.e., the maximum percentage of income spent or the poverty line used- when working with these methods is very influential on final outcomes. This thesis broadens the possible application of the impoverishment and catastrophic payment concepts



by applying them with (more readily available) macro data and investigating what impact using different methods and thresholds has on levels of affordability.

Over the last three decades the field of health economics has developed the tools and models to calculate the incremental costs and effects of health care interventions in cost-effectiveness analyses. The development of the Quality Adjusted Life Year, or QALY, has made it possible to compare the relative efficiency of interventions across different disease areas (Drummond et al., 2005). Although interventions delivering QALYs at lower cost may be considered more efficient than those delivered at a higher cost, the cost per QALY metric does not give insight in ‘the affordability’ of an intervention. The ratio only indicates at what price health can be bought through an intervention, but not whether this is deemed ‘value for money’. To answer the latter question, one needs to know how much a society is prepared to pay for health: the value attached to a QALY. This amount will probably depend on the income level of a country (as suggested by the World Health Organization<sup>3</sup>) and, hence, can be considered related to affordability. If the price per QALY exceeds what a society is willing and able to pay, the related intervention may be deemed unaffordable. Then, the opportunity costs in the form of other goals worthy of collective financing are simply too high. The actual value people place on one QALY or our willingness to pay for one year in full health is an increasingly researched topic (Culyer et al., 2007; McCabe et al., 2008; Pinto-Prades et al., 2009; Bobinac et al., 2010).

Most social insurance systems have developed criteria for determining the entitlements (basic benefit package) of the insured population (le Polain et al., 2010; Franken et al., 2012). Although efficiency arguments play a role in all these systems, not many countries (openly) ration on the basis of efficiency considerations. In the Netherlands the Dutch Health Care Insurance Board (CVZ) has developed a framework to delineate the basic benefit package. In this framework CVZ assesses the necessity for medical intervention and the studied technology’s effectiveness, efficiency and the feasibility (of it being implemented or included). The necessity criterion addresses the question whether the disease or required health care warrants a claim on solidarity. One of the reasons why this does not need to be the case is that people can afford to pay for the technology out-of-pocket. This thesis further refines the operationalization of the necessity criterion, as used in the context of delineating the Dutch basic benefits package.

Health economists also have advanced techniques to study equity in health care (Van Doorslaer et al., 1992; O’Donnell et al., 2008). This concerns not only the fair distribution of health (which can be defined as “the absence of systematic disparities in health between groups with different levels of underlying social advantage/

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3. [http://www.who.int/choice/costs/CER\\_thresholds/en/print.html](http://www.who.int/choice/costs/CER_thresholds/en/print.html)

disadvantage—that is, wealth, power, or prestige” (Braveman & Gruskin, 2003)), but also a fair distribution of health care and (financial) health care contributions. These issues may obviously be interrelated. In countries where OOP-payments account for a substantial portion of health care financing, wealth differences may cause differences in health care utilization and access, which may, in turn, lead to (unfair) differences in health. Research into equity in breast cancer care is relatively rare, especially in LMICs. This can partly be explained by the relatively high data requirements of such studies, which are not easily met in most LMICs (Parkin et al., 1999; Parkin et al., 2005; O’Donnell et al., 2008). In this thesis, the results of a study inquiring whether breast cancer treatment outcomes differ across socio-economic quintiles -i.e., people for whom treatment is more or less affordable- in an academic hospital in Ghana will be presented.

## 1.4 OUTLINE OF THE THESIS

### **PART I – Affordability at the micro level in low- and middle-income countries: the example of medicine affordability.**

The first part of this thesis focusses on the affordability of medicines in LMICs, which account for a large proportion of total health care costs in LMICs and are often paid for OOP. The work presented in this part results from a joint project with the World Health Organization (WHO) and Health Action International (HAI). WHO/HAI gathered information on medicine prices and availability in LMICs (Cameron et al., 2009b). Cameron et al. (2009b) did not use the aforementioned impoverishment or catastrophic payment methods to calculate the affordability of medicines. Instead, medicine affordability was expressed in terms of the days’ wages that a country’s Lowest Paid unskilled Government Worker (LPGW) needs to spend on a standard course of treatment (Cameron et al., 2009b). This metric, although perhaps easy to understand, does not clearly indicate (especially in country comparisons) for how many people a medicine is deemed unaffordable. This is especially due to the fact that the metric does not consider the income distribution in a country nor the fact that many people might earn less than the LPGW.

The application of the impoverishment and catastrophic payment methods requires micro data from household surveys. Because in LMICs these are not available on a yearly basis and are not conducted in a standardized way, the comparability of results across countries and over time is limited (Van Doorslaer et al., 2006; O’Donnell et al., 2008). In an attempt to address these limitations, in **chapter 2** the impoverishment and catastrophic payment methods are operationalized with macro data, which are more readily available. In **chapter 3** the impoverishment method as operationalized

with macro data is applied to calculate the affordability of four essential medicines in sixteen LMICs using poverty lines of US\$1.25 and US\$2.00 per day. **Chapter 4** then focusses on the importance and challenges that relate to the choice of when to consider something to be unaffordable when applying either the impoverishment or catastrophic payment method.

## **PART II – Affordability at the macro level in a developed country: delineating entitlements in social health insurance systems.**

Because increasingly expensive medical technology is an important reason for rising health care costs (Newhouse, 1992; Fuchs, 1996; Organization for Economic Co-operation and Development, 2006; Organization for Economic Co-operation and Development, 2010; Chandra & Skinner, 2012; Sorenson et al., 2013) delineating the basic benefit package in a stricter manner is a prime candidate to control the growth of health care expenditures in the Netherlands (Ham, 1997; Rijksoverheid, 2013). The discussion on how to do so, however, has been debated ever since the Dunning committee in 1991 published a report which proposed a methodology for this. Depicting the concepts of *necessity*, *effectiveness*, *efficiency* and *own account & responsibility* as sieves in a funnel, the committee argued that only those interventions passing through all four sieves of this funnel should enter the basic benefit package (Dunning A.J., 1991). Although there has been much support for these general principles, their definition and operationalization has been much debated and researched (e.g., Commissie Criteria Geneesmiddelenkeuze (chair: van Winzum), 1994; Wetenschappelijke Raad voor het Regeringsbeleid, 1997). In the Netherlands, CVZ is responsible for advising the Minister of Health on reimbursement decisions. It is good to note that its current decision framework is importantly based on Dunning's first three criteria (College voor Zorgverzekeringen, 2009a). The necessity criterion is now formed by two distinct sub-criteria: *disease burden* and *necessity of insurance*. To determine the *disease burden*, which is a measure of disease severity, CVZ applies the concepts of fair innings (Williams, 1997) and proportional shortfall (Stolk et al., 2004; Van de Wetering et al., 2013). Under the former, people are considered to be entitled to some 'normal' health achievement whereby those who do not meet this could receive more weight in health care decision making. According to the latter approach those people who stand to lose a larger proportion of their remaining health expectancy should be given priority in the decision making process. The sub-criterion of *necessity of insurance* concerns the question whether, from an individual viewpoint, insuring some intervention is necessary and appropriate. The operationalization of this criterion to date has not received much attention outside the field of medical aids (College voor Zorgverzekeringen, 2008a). **Chapter 5** introduces a framework

which aims to provide guidance, structure and transparency for the application of the *necessity of insurance* criterion, also in other health care domains.

### **PART III – Health economics at the macro level in low- and middle-income countries: choices in breast cancer and HIV/AIDS.**

While studying the affordability of health care services and systems at the micro and macro level provides useful insights for policy makers in both LMICs and high-income countries, in the end scarcity of resources requires choices. Part III of this thesis hence reports on the application of (health-economic) techniques that can be used to inform those choices. The last three studies again focus on LMICs where the burden of disease is typically higher than in high-income countries (Lopez et al., 2006) and the available per capita budget for health care is much lower (The World Bank Group, 2013c). Hence, an inefficient or unfair use of resources in these countries may have even larger effects on (the distribution of) population health than in high-income countries. Providing an optimal mix of health care interventions and ensuring that those needing them can access them, is an important goal in these countries which can be supported by scientific evidence. In **chapter 6** we use a general longitudinal population model (Lauer et al., 2003; Zelle et al., 2012) to calculate the costs and effects of various breast cancer interventions in Costa Rica and Mexico. After adjusting the model parameters to best resemble the breast cancer treatment and outcome situations in these countries, these cost-effectiveness analyses provide information for decision makers on how to further improve the breast cancer programs in their countries. Next, **chapter 7** reports on an equity study in Ghana, investigating whether patients from different socio-economic backgrounds experience different treatment outcomes from breast cancer care. Finally, **chapter 8** of this thesis sheds light on which policy areas need to be strengthened to tackle the HIV/AIDS epidemic in sub-Saharan Africa. While many studies focus on how various specific variables/policy areas impact HIV-prevalence, these variables/policy areas do not stand alone, i.e., they all influence HIV-prevalence simultaneously, perhaps offsetting each other. Therefore, we decided to take several variables from the United Nations' Human Development Reports and study if, and if so how, they simultaneously impacted changes in HIV-prevalence over a five-year span.

In **Chapter 9** the results from the individual chapters will be discussed and linked to the main research questions. Furthermore, their limitations will be debated and it will be shown how decision makers can use the outcomes presented in this thesis for policy making. Finally, future research questions will be identified.



# PART I

Affordability at the Micro Level in Low- and Middle-income Countries: The Example of Medicine Affordability





# Chapter 2

## Practical Measurement of Affordability: An Application to Medicines

Published as:

Niëns LM, Van de Poel E, Cameron A, Ewen M, Laing R, Brouwer WBF.

“Practical measurement of affordability: an application to medicines.”

*Bulletin of the World Health organization 2012 90(2): 219-227.*





## ABSTRACT

We use two practical methods for measuring the affordability of medicines in developing countries. The proposed methods –impoverishment and catastrophic payment methods– rely on easily accessible aggregated expenditure data and take into account a country's income distribution and absolute level of income. The catastrophic payment method quantifies the proportion of the population whose resources would be catastrophically reduced by spending on a given medicine; the impoverishment method estimates the proportion of the population that would be pushed below the poverty line by procuring a given medicine. These methods are illustrated by calculating the affordability of glibenclamide, an antidiabetic drug, in India and Indonesia. The results were validated by comparing them with the results obtained by using household micro data for India and Indonesia.

We find that when accurate aggregate data are available, the proposed methods offer a practical way to obtain informative and accurate estimates of affordability. Their results are very similar to those obtained with household micro data analysis and are easily compared across countries.

The impoverishment and catastrophic payment methods, based on macro data, can provide a suitable estimate of medicine affordability when the household level micro data needed to carry out more sophisticated studies are not available. Their usefulness depends on the availability of accurate aggregated data.

## 2.1 INTRODUCTION

Affordability is not an unequivocal concept; Bradley (2008) calls it vague, and Whitehead (1991), Milne (2006) and Komives et al. (2005) deny it having a clear basis in economic theory. The theory assumes that a household chooses the bundle of goods and services that maximizes utility -i.e. the benefit derived per money spent- subject to its preferences and budget. Clearly, different preferences lead to different choices on how much to spend on a particular commodity. The definition of what constitutes an “affordable” price is thus a normative one that, according to some, lacks an economic foundation (Stone, 2006). A commodity is obviously unaffordable if it costs more than what is in the full (potential) budget, but such a definition is overly restrictive.

According to MacLennan & Williams, describe affordability as securing a standard of living (e.g. housing, education or transport) at a price that “does not impose, in the eyes of a third party (usually government), an unreasonable burden on household incomes” (in: Hancock, 1993). To operationalize the concept of affordability, one therefore needs (i) information on household incomes; (ii) knowledge of the price of the commodity in question, and (iii) a definition of “unreasonable burden”. This highlights two problems related to measuring unaffordability. First, there is arbitrariness in defining “an unreasonable burden”. Previous work has identified two ways to define this unreasonable burden: (i) the so-called catastrophic payment method, which is based upon the ratio of the payment for a particular commodity to a household’s total resources, and (ii) the impoverishment method, which looks at a household’s residual income after paying for a good (Whitehead, 1991; Hancock, 1993; Carruthers et al., 2005; Kutty, 2005; Stone, 2006). The second problem is that measuring affordability in practice requires a large amount of household level data that is often difficult to access, only available for certain years, not comparable across different time periods or countries, or simply lacking.

To address the second problem while simultaneously acknowledging the first, in this paper we apply the impoverishment and catastrophic payment methods in a manner that can be applied to a broad range of commodities when micro data are scarce. We do this by applying these methods using widely available aggregate data, which makes for easy implementation and comparison across countries. We explore their use in elucidating the affordability of medicines, a commodity critically related to affordability. Indeed, in the developing world, medicines account for a substantial part of health-care costs (World Health Organization, 2000; World Health Organization, 2004b; Van Doorslaer et al., 2006; Cameron et al., 2009b). Since most of the population in many low-income countries lacks health insurance (Dror et al., 2002), medicines have to be paid for out of pocket when people fall ill. If their

prices are too high, people are unable to procure them and often forego treatment altogether or get into debt (Flores et al., 2008). It is therefore important to examine and compare the affordability of medicines across countries in the developing world and to monitor the impact of interventions seeking to improve it.

### **Measuring affordability**

As explained before, two approaches are generally used to estimate affordability. One relies on the ratio of expenditures to total household resources, whereas the second focuses on the residual income after an expenditure. Under the first approach, the payment for a commodity is deemed “catastrophic” (unaffordable) when it exceeds a certain proportion of a household’s resources. The idea is that if a household spends a large fraction of its available budget on a specific item, it will have to reduce its consumption of other goods and services. The affordability threshold is subjective (Hancock, 1993; Xu et al., 2003; Stone, 2006). Studies of this approach, which have focused primarily on the affordability of transportation (Carruthers et al., 2005), education (Murakami & Blom, 2008), health care (Wagstaff & Van Doorslaer, 2003; Xu et al., 2003) and utilities such as energy and water (Organization for Economic Co-operation and Development, 2003; Frankhauser & Tepic, 2005) define the affordability of a commodity in terms of the share of available resources that it consumes. Since spending even a small share of the budget can have catastrophic consequences for very poor individuals, it makes sense to define affordability in terms of the share of the budget that is left after spending on basic necessities (usually food). The latter has been referred to as “nondiscretionary expenditure” or “capacity to pay” (Wagstaff & Van Doorslaer, 2003; Xu et al., 2003).

The second or “impoverishment” method considers the absolute quantity of available resources before and after payment for a commodity. If the household is initially above the poverty line but drops below it after paying for the commodity, it can be said to have been “impoverished” by the payment (Dolbeare, 1966; Wagstaff & Van Doorslaer, 2003; Xu et al., 2003; Kutty, 2005). This approach has been commonly used to study housing affordability (Kutty, 2005; Stone, 2006) and has also been applied to health care (Wagstaff & Van Doorslaer, 2003; Xu et al., 2003). Niëns et al. (2010) have recently calculated the affordability of medicines in 16 low- and middle-income countries using this impoverishment method. The method is clearly more specifically focused on the poor within society, as the closer an individual is to the poverty line, the more likely it is that certain expenditures will push the individual below it.

The methods as operationalized by Xu et al. (2003) and Van Doorslaer et al. (2006), while theoretically optimal, may be difficult to apply in practice, especially in low- and middle-income countries, because they are relatively data intensive. This is particularly so if the goal is to monitor outcomes over time and make cross-country

comparisons. Comparisons across countries and over time are further complicated by the fact that individual household surveys suffer from methodological heterogeneity.

Aware of the problems inherent to measuring affordability, the World Health Organization (WHO) and Health Action International (HAI) have used the wage of the lowest paid unskilled government worker (LPGW) to calculate the affordability of medicines (World Health Organization & Health Action International, 2008; Cameron et al., 2009b). Such affordability has been expressed in terms of the number of days the LPGW has to work to be able to pay for a course of treatment with a particular drug. This LPGW-based metric is easy to apply and to understand; people in any country can easily position themselves relative to the LPGW. However, this metric may overestimate the affordability of medicines because a substantial proportion of the population in some countries earns less than the LPGW (Cameron et al., 2009b; Niëns & Brouwer, 2009; Niëns et al., 2010). Furthermore, the number of days of LPGW wages that makes something unaffordable is not clearly determined; this income metric is used only by WHO/HAI and no reference standards are available in the literature. As a result, the quest for a feasible way of applying the catastrophic payment and impoverishment methods in data-poor countries is amply justified.

In the remainder of this paper, we explain the methodological details of a less data-demanding and easily applicable operationalization of the catastrophic payment and impoverishment methods, and we illustrate them by calculating the affordability of glibenclamide, a drug for diabetes. For this purpose we have used data from a price survey undertaken with the WHO/HAI price measurement tool in India and Indonesia (World Health Organization & Health Action International, 2008). We then compare the results of applying this method with the results of theoretically similar calculations using household data.

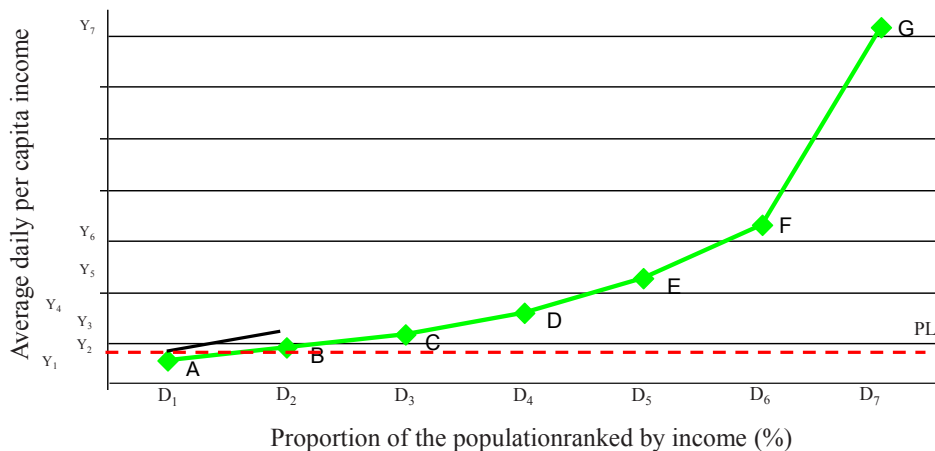
## 2.2 METHODS

Throughout this paper we refer to household level data as *micro data* and to aggregated data as *macro data*. The methods proposed in this paper only require aggregated data and are therefore referred to as *macro methods*, whereas methods typically calling for micro data are referred to as *micro methods*. To check the sensitivity of our proposed method to using different data, we produce results for several combinations of data and methods.

## Micro and macro methods

O'Donnell et al. (2008) elaborately explain how to calculate impoverishment and catastrophic payments at the household level using micro data. Other applications can be found in Van Doorslaer et al. (2006), Xu et al. (2003), Wagstaff and Van Doorslaer (2003) and Russell (2004).

The method for calculating medicine affordability that we propose in this paper requires a knowledge of four components: (i) the price of (treatment with) a given medicine ( $P$ ) (ii) a country's total population ( $Pop$ ); (iii) the aggregate income level of a country ( $Y$ ); and (iv) the proportion of the total income earned across income groups ( $D$ ) within a country. The last three components are first combined to draw an income distribution that plots the average daily income for each income group. Figure 1 shows an example of such a distribution. The x-axis ranks the total population ( $Pop$ ) by increasing income (income groups  $D_1$  to  $D_7$ ), whereas the y-axis plots the average daily incomes (groups  $Y_1$  to  $Y_7$ ). Because aggregated data are usually available for up to seven income groups, the explanation of our methods is based on this number, but the methods can be applied to more groups.



**Figure 1:** Distribution of average daily per capita income across income groups in Indonesia (2005)  
PL: Poverty Line

Note: The x axis ranks the total population by increasing income (income groups  $D_1$  to  $D_7$ ), whereas the y axis plots the average daily incomes (groups  $Y_1$  to  $Y_7$ ).

Since we have no information on how income is distributed within each income group, we assume linearity and plot the average income of each group at the midpoint, i.e., we assume that the mean and median incomes in each income group coincide. For example, for the income group between the 40th and 60th percentiles we plot the average income on the 50th percentile. This is clearly a simplification.

In reality, the income distribution within each income group is likely to be skewed because most people in the group probably earn less than the average. This means that we are likely to overestimate the average income for each income group and therefore to underestimate the affordability of the medicine later on in the analysis.

### The impoverishment approach

This method aims to compare the proportion of the population below the poverty line (PL) before ( $I_{pre}$ ) and after ( $I_{post}$ ) the hypothetical procurement of a medicine. Assume that line PL in Figure 1 represents the poverty line in a specific country. To calculate the proportion of the population living below this line, we focus on the income distribution between two income points, one just below and the other just above the poverty line, in this case *A* and *B*. With the coordinates of these points known [i.e., for *A*, ( $D_1, Y_1$ ); for *B*, ( $D_2, Y_2$ )], we can calculate the linear function of the (thick black) line going through *A* and *B* (Equation 1:  $Y = \frac{Y_2 - Y_1}{D_2 - D_1} D + C$ ) which allows us to estimate the proportion of the population living below the poverty line ( $I_{pre}$ ).

To estimate the proportion of the population below the poverty line after purchasing a medicine,  $I_{post}$ , we assume a parallel shift downwards of the linear function equal to the medicine price *P*. Equation 1 then changes into Equation 2:

$$Y' = \frac{Y_2 - Y_1}{D_2 - D_1} D + C - P$$

Again, substituting  $Y'$  by PL in this Equation 2 gives us  $I_{post}$ , the proportion of the population in poverty after procurement of the medicine. The difference in the proportion of the population below the PL before and after paying *P*,  $I_{post} - I_{pre}$ , gives the proportion of the population that would be impoverished if everyone had to buy a medicine costing *P*. For the percentage of the population represented by  $I_{post}$  the medicine is deemed unaffordable.

### The catastrophic payment approach

In the existing literature, total health care expenditures are usually considered catastrophic if they exceed 10% of a household's total spending or 40% of non-food spending (Prescott, 1999; Ranson, 2002; Wagstaff & Van Doorslaer, 2003; Xu et al., 2003; McIntyre et al., 2006; O'Donnell et al., 2008).

In developing countries, such as India and Indonesia, medicines make up a relatively large portion (20–70%) of total health expenditure and are paid largely out of pocket (World Health Organization, 2000; World Health Organization, 2004b; Van Doorslaer et al., 2006). According to data from WHO's 2003 World Health Survey for India, drug spending in the country accounts for about 44% of all out-of-pocket

spending on health. Low health insurance coverage in Indonesia (26.1% in 2007) and India (approximately 20%) indicate that most spending on medicines is paid for out of pocket (World Health Organization, 2003; Roxk et al., 2009).

Hence, to calculate the affordability of medicines we propose using a threshold that is roughly half the threshold generally used when calculating total health care expenditure, i.e., 5% instead of 10%. However, the method can obviously accommodate different percentages.

The proportion of the population for which purchasing a medicine costing  $P$  is catastrophic is again calculated from Figure 1. At a 5% catastrophic threshold, the medicine with price  $P$  is unaffordable for people earning less than 20 times  $P$ . This proportion is again calculated by drawing a line between the points for average income that include  $20P$ . By substituting  $Y$  by  $20P$  in Equation 1, we get the proportion of the population exposed to catastrophic payments,  $X_{cat}$ .

### Data sources

We obtained medicine prices from the WHO/HAI database, which lists median treatment prices for a large range of medicines. WHO/HAI collects medicine prices from five medicine outlets per sector in at least four geographic or administrative regions in a given survey area. For each medicine, prices are collected for both the originator brand (OB) and the lowest-priced generic (LPG) equivalents in the private and public sectors. We use private sector prices because drug availability in the public sector is low and the data are often insufficient to make reliable price estimates (Cameron et al., 2009b; Niëns et al., 2010).

In our examples we use the price of 5-mg capsules/tablets of the LPG glibenclamide in India (April 2003 – January 2005) and Indonesia (August 2004) and assume the standard treatment regimen of 2 tablets a day. We chose these two countries because of the availability of micro, macro and medicine price data. We selected glibenclamide because in India and Indonesia diabetes affects 50.7 million and 6.9 million people (4.6% and 7.1% prevalence, respectively) (International Diabetes Federation, 2010).

When the lowest-priced generic equivalent of glibenclamide is procured in the Indonesian private sector, the median price of treatment with the drug is 417 Indonesian rupiah (IDR) a day. For India, seven WHO/HAI surveys are available, and each covers a state or part of a state. As the price of LPG glibenclamide in the private sector varies little (between 1.28 and 1.60 Indian rupees (INR) a day) and given the aim of this paper, we work with the average price of LPG glibenclamide over the seven surveys, i.e., INR 1.40.

The aggregate income level ( $Y$ ) and income distribution of India and Indonesia are retrieved from the World Bank's World Development Indicators (WDIs). Gross domestic product (GDP) per capita is often used as a proxy for people's actual incomes.

However, a country's GDP consists of consumption, gross investment, government spending and net trade. For this study the main interest lies in consumption, since it reflects the amount of money people can actually spend. Therefore, household final consumption expenditure as provided in the WDIs, is used. This is in line with micro-level analysis, in which expenditure data are usually preferred to income data because the former are believed to better reflect household resources in developing countries (O'Donnell et al., 2008). As for income distribution  $D$ , the WDIs provide the percentage of total income earned in seven income groups: five quintiles, with the upper and lower quintiles split into two deciles each.

We use the 2005 PL thresholds of 1.25 and 2.00 United States dollars (US\$) a day, as suggested by the World Bank (The World Bank Group, 2010; The World Bank Group, 2013c). We convert the PL thresholds to 2005 Indonesian rupiahs (IDR 4917 and IDR 7869) and 2000 Indian rupees (INR 18.20 and INR 29.12) with conversion factors from the World Bank International Comparison Program (The World Bank Group, 2011a). We perform all calculations of  $I_{\text{pre}}, I_{\text{post}} - I_{\text{pre}}$  and  $X_{\text{cat}}$  in local currency units, but we express all prices and amounts in this paper in 2005 purchasing power parity US\$.

To check the robustness of our results, we also calculate the affordability of LPG glibenclamide using micro data from the 2005 wave of the Indonesian National Socioeconomic Survey (Susenas) ( $n = 7302$  households) and the Indian National Sample Survey (NSS) data set from 2000 (round 55) ( $n = 93854$  households). These surveys collect information on total household expenditures through an extensive expenditure module in the household survey (Ministry of Statistics and Program Implementation, 2011; RAND Corporation, 2011).

## 2.3 RESULTS

### Micro data

Table 1 shows the results of the calculations based on micro data. In Indonesia the proportions of the population living below the US\$ 1.25 and US\$ 2.00 PLs ( $I_{\text{pre}}$ ) are 28.8% and 61.7%, respectively. The proportions of the population at risk of being impoverished by procuring LPG glibenclamide ( $I_{\text{post}} - I_{\text{pre}}$ ) are 5.8% and 3.7%, respectively. The catastrophic payment approach shows the proportion at risk of being confronted with catastrophic payments ( $X_{\text{cat}}$ ) to be 65.9%.

In India, the proportion of people living below the US\$ 1.25 and US\$ 2.00 PLs ( $I_{\text{pre}}$ ) is 53.0% and 80.4%, respectively. The impoverishment rates ( $I_{\text{post}} - I_{\text{pre}}$ ) in the country are 5.1% and 1.9%, and the proportion of the population at risk of catastrophic payments ( $X_{\text{cat}}$ ) is 78.6%.



**Table 1:** Proportion (%) of population impoverished or at risk of incurring catastrophic payments by purchasing treatment with lowest-priced generic equivalent of glibenclamide, by micro method using micro data for India and Indonesia

Country (source)	Below PL before medicine purchase ( $I_{pre}$ )		Impoverished by medicine purchase ( $I_{post} - I_{pre}$ ) <sup>a</sup>		Catastrophic payment ( $X_{cat}$ ) <sup>b</sup>
<b>Indonesia (WDI 2005)</b>					
PL threshold	< US\$ 1.25 <sup>c</sup>	< US\$ 2.00 <sup>d</sup>	< US\$ 1.25 <sup>c</sup>	< US\$ 2.00 <sup>d</sup>	
% of population	28.8	61.7	5.8	3.7	65.9
<b>India (WDI 2000)</b>					
PL threshold	< US\$ 1.25 <sup>c</sup>	< US\$ 2.00 <sup>d</sup>	< US\$ 1.25 <sup>c</sup>	< US\$ 2.00 <sup>d</sup>	
% of population	53.0	80.4	5.1	1.9	78.6

$I_{post}$ , percentage of the population below the poverty line after expenditure;  $I_{pre}$ , percentage of the population below the PL before expenditure; WDI, World Bank world development indicators;  $X_{cat}$ , percentage of the population at risk of incurring catastrophic payments at a threshold of 5% of per capita household expenditures.

<sup>a</sup> Impoverishment method.

<sup>b</sup> Catastrophic payment method.

<sup>c</sup> Purchasing power parity United States dollars (2005).

<sup>d</sup> Purchasing power parity United States dollars (2005).

## Macro data

Table 2 shows the results of using the aggregate income, as measured by the household final consumption expenditure ( $Y$ ), the proportion of total income earned across income groups ( $D$ ) and the total population (Pop) to calculate the daily average income per capita for each income group in India and Indonesia.

Dividing  $Y$  by Pop to derive per capita income estimates relies on the assumption that the average household size is constant across income groups. Since poorer households are typically larger (Lipton & Ravallion, 1994), the average income per capita is likely to be overestimated in the lower income distribution ranges, which should make our affordability estimates conservative.

In Indonesia, the daily cost of the standard treatment with LPG glibenclamide is US\$ 0.11, so individuals earning between US\$ 1.25 and US\$ 1.35 and between IDR US\$ 2.00 and US\$ 2.10 are at risk of being pushed below the US\$ 1.25 and US\$ 2.00 PLs, respectively, should they have to buy glibenclamide. In India, where the cost of LPG glibenclamide is US\$ 0.10, the individuals at risk of being pushed below the US\$ 1.25 and US\$ 2.00 PLs are those whose income ranges between US\$ 1.25 and US\$ 1.34 and between US\$ 2.00 and US\$ 2.09, respectively.

**Table 2:** Use of aggregated income and population data to calculate average daily income per capita (IPC) in specific income groups in India and Indonesia

Cumulative % of population <sup>a,b</sup>	Income group	India (WDI 2000)		Indonesia (WDI 2005)	
		Income distribution (%)	Average daily IPC (INR <sup>c</sup> )	Income distribution (%)	Average daily IPC (IDR <sup>d</sup> )
D <sub>1</sub> 0–10	Poorest 10%	3.64	13.21	3.00	6,649
D <sub>2</sub> 10–20	Second poorest 10%	4.44	16.11	4.15	9,209
D <sub>3</sub> 20–40	Second 20%	11.27	20.45	10.74	11,914
D <sub>4</sub> 40–60	Third 20%	14.94	27.11	14.38	15,949
D <sub>5</sub> 60–80	Fourth 20%	20.37	36.96	20.45	22,683
D <sub>6</sub> 80–90	Second richest 10%	14.21	51.56	14.96	33,172
D <sub>7</sub> 90–100	Richest 10%	31.13	112.96	32.32	71,679

WDI, world development indicators (World Bank).

<sup>a</sup> In 2005 purchasing power parity United States dollars, aggregate income level (Y) for Indonesia is \$425,869,484,516; Y for India is \$1,046,538,703,424.

<sup>b</sup> Population of Indonesia: 220 558 000; population of India: 1 015 923 000.

<sup>c</sup> 1US\$ = 14.56 INR.

<sup>d</sup> 1US\$ = 3934 IDR.

Table 3 shows the results of calculations based on macro methods and macro data. The differences are graphically presented in Figure 2. For India, the figure displays the two poverty lines and the average daily incomes per capita based on the macro and micro data and methods. The proportions of the population below the US\$ 2.00 PL are indicated with vertical lines from both the square and the triangle.

**Table 3:** Proportion (%) of population impoverished by or at risk of incurring catastrophic payments by purchasing treatment with lowest-priced generic equivalent of glibenclamide, by macro method using macro data for India and Indonesia

Country/year	Below PL before medicine purchase ( $I_{pre}$ )		Impoverished by medicine purchase ( $I_{post} - I_{pre}$ ) <sup>a</sup>		Catastrophic payment ( $X_{cat}$ ) <sup>b</sup>
<b>PL thresholds</b>	US\$ 1.25 <sup>c</sup>	US\$ 2.00 <sup>d</sup>	US\$ 1.25	US\$ 2.00	
Indonesia (2005)	0.0	9.8	0.0	1.6	11.6
<b>PL thresholds</b>	US\$ 1.25 <sup>c</sup>	US\$ 2.00 <sup>d</sup>	US\$ 1.25	US\$ 2.00	
India (2000)	22.2	54.1	4.8	2.8	51.8

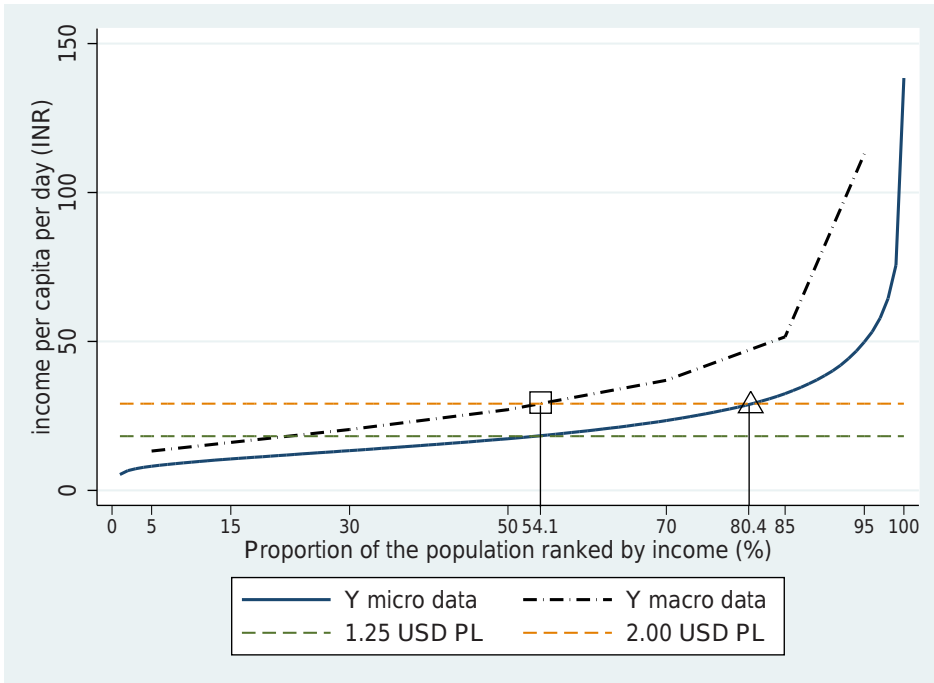
$I_{post}$ , percentage of the population below the poverty line after expenditure;  $I_{pre}$ , percentage of the population below the PL before expenditure;  $X_{cat}$ , percentage of the population at risk of incurring catastrophic payments at a threshold of 5% of per capita household expenditures.

<sup>a</sup> Impoverishment method.

<sup>b</sup> Catastrophic payment method.

<sup>c</sup> Purchasing power parity United States dollars (2005).

<sup>d</sup> Purchasing power parity United States dollars (2005).



**Figure 2:** Poverty lines and incomes for India based on macro and micro data and methods  
 Note: The x-axis lists the middle of the income group percentiles used with the macro approach to plot our graph. As such, the graph based on macro data begins and ends at the 5th and 95th percentiles, respectively. The proportions of the population below the US\$ 2.00 PL are indicated with vertical lines from both the square and the triangle.

There are large differences between  $I_{pre}$  poverty estimates and World Bank WDIs. For Indonesia, the World Bank's poverty estimates for 2006 are 28.04% (US\$ 1.25 PL) and 62.76% (US\$ 2.00 PL), whereas for India (2005) they are 41.6% (US\$ 1.25 PL) and 75.6% (US\$ 2.00 PL) (The World Bank Group, 2013c). These estimates closely resemble the figures obtained using the micro method and micro data (Table 1), but not the ones ( $I_{pre}$ ) obtained using the macro method and macro data (Table 3).

For each PL in Indonesia, the proportion of the population impoverished by the purchase of glibenclamide ( $I_{post} - I_{pre}$ ) is lower when calculated with the macro method and data (US\$ 1.25 PL: 0.0%; US\$ 2.00 PL: 1.6%; Table 3) than when calculated with the micro method and data (US\$ 1.25 PL: 5.8%; US\$ 2.00 PL: 3.7%; Table 1). In India, the proportion impoverished ( $I_{post} - I_{pre}$ ) is lower only for the US\$ 1.25 PL (4.8% versus 5.1%; Table 1), not for the US\$ 2.00 PL (2.8% versus 1.9%; Table 1). This is because in India the US\$ 2.00 PL, here measured with the macro methods, is now located in a lower income region (the region marked with a square in Figure 2) where  $D$  is less skewed -i.e., compared with the region marked with a triangle in Figure 2. In other

words, the linear line in the region marked with a square is slightly flatter than the convex income distribution ( $D$ ) in the region marked with a triangle, which causes the shift over  $D$  to be larger for the same parallel drop of the linear function.

In both countries, the proportion of the population at risk of being confronted with catastrophic spending by purchasing glibenclamide ( $X_{cat}$ ) differs substantially when calculated with the micro and macro approaches. While with the former, the proportion is 65.9% for Indonesia and 78.6% for India (Table 1), the latter approach gives proportions of 11.6% and 51.8% respectively (Table 3).

The results so far illustrate that the affordability of treatment with glibenclamide in India and Indonesia varies markedly depending on the method used to calculate it, but both the micro and macro approaches show that its affordability poses problems in both countries. The differences in the results obtained with the two methods may reflect a *methodological effect* or a *data effect*. We investigated this in more detail and found that while the methodological effect is negligible, the data effect is real, i.e., differences in micro and macro data account for the differences in the results found (Appendix).

## 2.4 DISCUSSION

The issue of affordability is not straightforward. Although it is a rather normative concept (Stone, 2006), this paper has explored two methods for estimating the affordability of medicines in low- and middle-income countries: the catastrophic payment and the impoverishment method. To ensure their practical applicability, both were designed for use with aggregated data on medicine prices, per capita income level, and income distribution that are easily available for a broad set of developing countries from the WDIs and the WHO/HAI medicine price database. This facilitates the measurement, comparison and monitoring of affordability in a range of countries over time, as illustrated by Niëns et al. (2010). Clearly, the use of aggregated data does require some simplifying assumptions. For instance, in our study we have conservatively assumed per capita income to be linearly distributed across income groups, which is likely to generate bias and lead to lower affordability results. Other assumptions can be made in a relatively straightforward manner (e.g. by fitting a distribution line to the observed points). Worthy of note is that the methods presented here assess the catastrophic and impoverishing effects of *hypothetical* expenditures on medicines. In this setting, a medicine is considered 100% affordable if everyone can procure it without experiencing financial hardship.

This study has some limitations. First, the usefulness of the proposed aggregated method depends largely on the validity of the aggregated income data. We found the WDI's household final consumption expenditure estimates to be substantially higher than the income data collected in household surveys, a finding in line with Ravallion's observation that income data from household surveys for 88 countries with national accounts were lower 77% of the time (Ravallion, 2003). Thus, the use of macro methods leads to impoverishment rates that are lower than expected most of the time. Although household survey data generally yield the most precise estimates of affordability, total expenditure estimates from household surveys also differ because of differences in survey structure and in the questions asked (Lu et al., 2009; Xu et al., 2009).

A more general limitation of our study is that it focuses on the affordability of a single medicine, which obviously ignores the need for more than one medicine and for other therapeutic methods in some cases, as well as related costs, such as fees for physician visits. However, our objective was not to provide a measure of treatment affordability as a whole, but only of medicine affordability. Since medicines account for a large portion of total treatment costs in low- and middle-income countries (World Health Organization, 2000; World Health Organization, 2004b; Van Doorslaer et al., 2006; Cameron et al., 2009b), their cost is largely indicative of people's ability to afford the treatment for specific diseases.

Another limitation is the choice of the thresholds used to define impoverishment and catastrophic payments. Such a choice obviously influences the affordability outcomes and cannot be unambiguously defined. The impoverishment method calls for defining a threshold below which people are considered to be impoverished. Although the thresholds used in our study are well accepted and commonly applied, even in the context of global development initiatives, including the Millennium Development Goals (United Nations, 2010), they are ultimately based on normative choices regarding minimum human requirements in areas such as housing and nutrition. Many countries have defined their own poverty lines and these could also be used in this context, since the absolute threshold required for use of the impoverishment method should reflect the living standards in a given country. The thresholds employed for the catastrophic payment method are even more arbitrary. We therefore recommend using a range of thresholds when applying the catastrophic payment method. The *level* of analysis should also be considered when setting a threshold. For instance, the relevant threshold may be set lower when assessing the affordability of individual medicines rather than total health-care expenditures. It is important that such choices be explicitly justified within studies.

The methods proposed in this paper allow for a more accurate estimate of affordability than the LPGW method when reliable aggregated expenditure data are avail-

able to mitigate the *data effect*. The *methodological effect* is negligibly small when macro methods are used, but the *data effect* can be sizable. Thus, using the WDI's household final consumption expenditures as a proxy for expenditures at the aggregate level can be useful in identifying trends in the affordability of medicines or other commodities, but the absolute numbers have to be interpreted with caution. If better aggregated data -i.e., data that is closer to estimates from household surveys- are available, the proposed macro methods allow for quite reliable affordability estimates. We have for example used aggregated spending indicators from India's Planning Commission web site (Government of India, 2010) for Maharashtra state and confirmed affordability estimates to be very close to those based on household NSS data. (The results are available from the corresponding author upon request.)

A critique to the LPGW approach is that it may tend to overestimate affordability, as in many countries a substantial proportion of the population earns less than the LPGW. This was confirmed by our data. Using the micro method with micro data we find 95.5% of the population earns less than the LPGW in Indonesia, in India this percentage is 99.8%. In Indonesia, the average LPGW wage was IDR 20 700 a day in 2004 (WHO/HAI survey). In India, the average LPGW wage over the seven WHO/HAI surveys was INR 133.81 (range: 120.00–143.93).

The two methods described herein, which are conceptually different, present ample opportunities for future research. Which method should be applied depends to a great extent on a particular country's economic situation. When a large percentage of the population has a pre-payment income below the poverty line, the impoverishment method is useful only if this percentage is known. On the other hand, the catastrophic payment method does not capture to what extent, if at all, the "catastrophic" payments on medicines actually cause poverty and hardship. Very rich households can spend a "catastrophic" percentage of their income on medicines without experiencing any financial difficulties. Again, affordability is a vague concept and its measurement requires some normative assumptions. This paper's purpose was not to impose particular assumptions, but rather to propose measurement tools that can be easily applied in settings where detailed household-level data are limited or unavailable to operationalize the concept of affordability, whether they are applied to medicines or to other health commodities. Such methods are particularly helpful in comparing affordability across countries or over time and their use can provide policy-makers with useful insights into people's purchasing power in relation to the cost of medicines.

## APPENDIX

### Macro versus micro data

Table 4 displays the average incomes for seven income groups ( $D_1$  to  $D_7$ ) calculated from the micro Susenas (Indonesia) and NSS (India) data sets (columns A and D). We calculated the incomes in columns B and E by aggregating total household incomes from the micro data and applying the WDI income distributions for 2005, i.e., as in Table 2. Finally, for comparison, columns C and F in Table 4 present the same incomes that are listed in Table 2.

The results presented in Table 4 clearly show that the average incomes obtained from the macro data are much higher (by a factor 1.5 to 2.5) than the ones obtained from the micro data. This can explain the low poverty estimates obtained when calculations are based on macro data.

**Table 4:** Average incomes (Indonesia and India) per income group for micro & macro level data with both micro and macro income distributions

Income group	Indonesia (IDR)			India (INR)		
	Income source (Y)	Micro <sup>a</sup>	Macro	Micro <sup>b</sup>	Macro	Macro
Distribution (D)	Micro <sup>a</sup>	Macro	Macro	Micro <sup>b</sup>	Macro	Macro
	A	B	C	D	E	F
$D_1$ - Poorest decile	2,876	2,556	6,649	7.96	8.13	13.21
$D_2$ - Second poorest 10%	3,908	3,540	9,209	10.63	9.91	16.11
$D_3$ - Second 20%	5,008	4,580	11,914	13.46	12.58	20.45
$D_4$ - Third 20%	6,666	6,131	15,949	17.58	16.68	27.11
$D_5$ - Fourth 20%	9,073	8,720	22,683	23.95	22.74	36.96
$D_6$ - Second richest 10%	12,755	12,752	33,172	33.33	31.73	51.56
$D_7$ - Richest 10%	24,407	27,554	71,679	60.78	69.51	112.96

IDR, Indonesian rupiah; INR, Indian rupee; Macro, based on the World Bank's World Development Indicators.

<sup>a</sup> Susenas.

<sup>b</sup> NSS.

### Macro methods applied to micro data

To further investigate whether the different results could be reflecting methodological differences, we applied macro methods to the aggregate incomes as computed from micro data (columns A, B, D, E in Table 4) to calculate the proportion of the population below the PL ( $I_{pre}$ ), the rates of impoverishment ( $I_{post} - I_{pre}$ ) and the proportion at risk of facing catastrophic payments ( $X_{cat}$ ) (Table 5). To see if the income

distribution (D) used caused the results to differ, we calculated D with both micro and macro data sets.

When we applied macro methods to micro data (both Y and D), the proportion of the population living below the PLs ( $I_{pre}$ ) in both India and Indonesia was found to be lower than when we applied micro methods to micro data (Table 1). In Indonesia,  $I_{pre}$  was 28.8% and 60.0% respectively. In India  $I_{pre}$  was 51.9% and 78.3%, respectively (Table 5, Panel A).

**Table 5:** macro methods on micro data

**Panel A:** Proportion below PL

Distribution (D) from		Below PL before medicine purchase ( $I_{pre}$ )			
		micro		macro	
Year	country / PLs	US\$ 1.25 <sup>c</sup>	US\$ 2.00 <sup>d</sup>	US\$ 1.25	US\$ 2.00
2005	Indonesia <sup>a</sup>	28.8%	60.0%	34.4%	63.4%
2000	India <sup>b</sup>	US\$ 1.25 <sup>c</sup>	US\$ 2.00 <sup>d</sup>	US\$ 1.25	US\$ 2.00
		51.9%	78.3%	55.0%	80.6%

$I_{pre}$ , percentage of the population below the PL before expenditure

<sup>a</sup> Susenas.

<sup>b</sup> NSS.

<sup>c</sup> Purchasing power parity United States Dollars (2005).

<sup>d</sup> Purchasing power parity United States Dollars (2005).

**Panel B:** impoverishment rates ( $I_{post} - I_{pre}$ ) & catastrophic payments ( $X_{cat}$ ) at 5% of an individual's total resources

Distribution (D) from		Impoverished by medicine purchase ( $I_{post} - I_{pre}$ ) <sup>c</sup>			
		Micro		Macro	
Year	Country /PLs	US\$ 1.25	US\$ 2.00	US\$ 1.25	US\$ 2.00
2005	Indonesia <sup>a</sup>	5.7%	3.5%	5.4%	3.2%
		US\$ 1.25	US\$ 2.00	US\$ 1.25	US\$ 2.00
2000	India <sup>b</sup>	4.4%	2.2%	4.6%	2.3%
		Catastrophic payment ( $X_{cat}$ ) <sup>d</sup>			
2005	Indonesia <sup>a</sup>	63.9%		68.1%	
2000	India <sup>b</sup>	76.4%		78.8%	

$I_{post}$ , percentage of the population below the poverty line after expenditure;  $I_{pre}$ , percentage of the population below the PL before expenditure; WDI, World Bank world development indicators;  $X_{cat}$ , percentage of the population at risk of incurring a catastrophic payment at a threshold of 5% of per capita household expenditures.

<sup>a</sup> Susenas.

<sup>b</sup> NSS.

<sup>c</sup> Impoverishment method.

<sup>d</sup> Catastrophic payment method

<sup>c</sup> Purchasing power parity United States Dollars (2005).

<sup>d</sup> Purchasing power parity United States Dollars (2005).



Impoverishment rates ( $I_{post} - I_{pre}$ ; see Table 5 Panel B) in Indonesia (5.7% and 3.5%, respectively, for the US\$ 1.25 and US\$ 2.00 PLs) were lower than when we applied micro methods to micro data (Table 1). In India, Impoverishment rates ( $I_{post} - I_{pre}$ ) are only lower at the US\$ 1.25 USD PL, i.e., 4.4% compared to 5.1% in Table 1. However, at the US\$ 2.00 PL we find  $I_{post} - I_{pre}$  to be higher -i.e., 2.2% compared to 1.9% in Table 1- when applying the macro methods. The explanation for this is that a parallel shift downwards of the linear function in Fig. 1 (macro methods) causes a larger shift over the income distribution ( $D$ ) than when using the real  $D$  with a convex curve (micro methods), because the latter is steeper between higher income groups. Thus, whereas the macro methods cause the proportion below the poverty line ( $I_{pre}$ ) to be lower, this is not necessarily the case for the impoverishment rate ( $I_{post} - I_{pre}$ ), especially in higher income regions where the convex curve likely will be steeper. The proportion of the populations in Indonesia and India at risk of catastrophic payments drops to 63.9% and 76.4%, respectively (compared to 65.9% and 78.6% in Table 1).

Using the income distribution ( $D$ ) from the macro data shows the results to be slightly different. In Indonesia the proportion below the poverty line ( $I_{pre}$ ) increases slightly to 34.4% and 63.4% and the impoverishment rates ( $I_{post} - I_{pre}$ ) drop further to 5.4% and 3.2%. In India  $I_{pre}$  also increases to 55.0% and 80.6% below the PLs of US\$ 1.25 and US\$ 2.00, respectively. However,  $I_{post} - I_{pre}$  for the two poverty lines increases to 4.6% and 2.3%. For both Indonesia and India, up to income group  $D_6$ , (apart from  $D_1$  in India) all the average incomes in columns B and E are lower than those in columns A and D. For income group  $D_7$  it is the other way around. Thus, compared to the micro income distribution ( $D$ ), in this case  $D$  from the WDIs is more skewed in favour of the rich. As a result the proportion below the PLs ( $I_{pre}$ ) and the proportion confronted with catastrophic payments ( $X_{cat}$ ) are higher. For the impoverishment rates ( $I_{post} - I_{pre}$ ) on the other hand, this does not matter much as this figure does not depend on the absolute level of the income (but a shift over the same income distribution). The reasons for  $I_{post} - I_{pre}$  to be higher for the 2.00 USD PL in India is the same as explained in the previous paragraph, i.e., the parallel shift equal to the price of a medicine ( $P$ ) over a linear line takes up a larger portion of the income distribution  $D$  than the same shift over a convex curve.

The proportion of the populations in Indonesia and India at risk of catastrophic payments increases to 68.1% and 78.8% respectively (compared to 65.9% and 78.6% in Table 1).

## LETTER TO THE EDITOR: BETTER MEASURES OF AFFORDABILITY REQUIRED

A. Cameron and colleagues (Cameron et al., 2009b) address the important topic of affordability of medicines in low-income and middle-income countries. The magnitude of the affordability problem depends on medicine prices *and* on the income level and distribution in a country. Regarding income level, a convenient yet uncommon metric is used by Cameron and colleagues -i.e., the salary of the lowest-paid unskilled government worker (LPGW). Use of this unusual measure hampers the interpretation of results and might overestimate the affordability of medicines. As they acknowledge, often “a substantial proportion of the population” earns less than the LPGW. In collaboration with WHO and Health Action International, we investigated this situation in 17 of the countries in the Cameron study (Niëns et al., 2009). It turned out that, in 13 of these countries, half or more of the population was actually able to spend (much) less than the LPGW. The LPGW therefore is relatively well-off in most countries and at least half of the population in the 13 countries needs to work more days than the LPGW to pay for necessary medicines. Using household expenditure data and income distributions, we applied more common measures of affordability of medicines, based on impoverishment -i.e., earning less than US\$1 or \$2 per day- and catastrophic spending on medicines, i.e., more than a certain proportion of total spending (Hancock, 1993; Wagstaff & Van Doorslaer, 2003). Our results highlight that the already compelling results shown by Cameron and colleagues are, in fact, substantial overestimates of the affordability of medicines. Unfortunately, therefore, even more people lack financial access to necessary medicine, stressing the need for intervention.

Published as:

Niëns LM, Brouwer WBF, “Better measures of affordability required” *Lancet* 2009, March 28; 373 (9669):1081 – Letter to the Editor



# Chapter 3

## Quantifying the Impoverishing Effects of Purchasing Medicines: A Cross-Country Comparison of the Affordability of Medicines in the Developing World

Published as:

Niëns LM, Cameron A, Van de Poel E, Ewen M, Brouwer WBF, Laing R  
"Quantifying the Impoverishing Effects of Purchasing Medicines: A Cross-Country Comparison of the Affordability of Medicines in the Developing World."

*PLoS Medicine* 2010 7(8): e1000333.doi:10.1371/journal.pmed.1000333



## ABSTRACT

Increasing attention is being paid to the affordability of medicines in low- and middle-income countries (LICs and MICs), where medicines are often highly priced in relation to income levels. The impoverishing effect of medicine purchases can be estimated by determining pre- and post-payment incomes, which are then compared to a poverty line. Here we estimate the impoverishing effects of four medicines in sixteen LICs and MICs using the impoverishment method as a metric of affordability.

Affordability was assessed in terms of the proportion of the population being pushed below US\$1.25 or US\$2 per day poverty levels because of the purchase of medicines. The prices of salbutamol 100mcg/dose inhaler, glibenclamide 5mg cap/tab, atenolol 50mg cap/tab and amoxicillin 250mg cap/tab, were obtained from facility-based surveys undertaken using a standard measurement methodology. The World Bank's World Development Indicators provided household expenditure data and information on income distributions. In the countries studied, purchasing these medicines would impoverish large portions of the population (up to 86%). Originator brand products were less affordable than lowest-priced generic equivalents. In the Philippines, for example, originator brand atenolol would push an additional 22% of the population below USD1.25 per day, whereas for the lowest priced generic equivalent this is 7%. Given related prevalence figures, substantial numbers of people are affected by the unaffordability of medicines in practice.

Comparing medicine prices to available income in LICs and MICs shows that medicine purchases by individuals in those countries could lead to the impoverishment of large numbers of people. Action is needed to improve medicine affordability, such as promoting the use of quality assured, low-priced generics, and establishing health insurance systems.

### 3.1 INTRODUCTION

In developing countries the cost of medicines accounts for a relatively large portion of total healthcare costs (World Health Organization, 2000; World Health Organization, 2004b; Van Doorslaer et al., 2006; Cameron et al., 2009b). As the majority of people in developing countries do not have health insurance (Dror et al., 2002) and medicines provided free through the public sector are often unavailable (Cameron et al., 2009b), medicines are often paid for out-of-pocket at the time of illness. Consequently, where medicine prices are high, people may be unable to procure them and forego treatment or they may go into debt. For this reason, the World Health Organization (WHO) has designated affordable prices as a determinant of access to medicines (together with rational selection and use, sustainable financing, and reliable health and supply systems) (World Health Organization, 2008a). In several international treaties, access to healthcare is laid down as a right (United Nations General Assembly, 1948; United Nations Office of the High Commissioner for Human Rights, 1966). States have a legal obligation to make essential medicines available to those who need them at an affordable cost. Determining the degree of affordability of medicines, especially in low- and middle-income countries (LICs and MICs), is an important, yet complex undertaking as affordability is a vague concept.

Medicine affordability has been investigated in terms of the days' wages that a country's lowest paid unskilled government worker (LPGW) needs to spend on a standard course of treatment (World Health Organization & Health Action International, 2008; Cameron et al., 2009b). However, this metric is limited in that it does not provide insight into the affordability of medicines for the often large sections of the population that earn less than the LPGW (Cameron et al., 2009b; Niëns & Brouwer, 2009). Recently, Niëns et al. (2009) have proposed two alternative methods to gain insight into the affordability of medicines in the developing world. A first method focuses on the catastrophic impact of expenditures on medicines, while the second approach consists of studying the impoverishing effect of these expenditures. This paper discusses the application of the latter approach and presents the results of a cross-country analysis of the affordability of four medicines in 16 developing countries.

### 3.2 METHODS

Our measurement of the affordability of medicines is based on the approach taken by Van Doorslaer et al. (2006), who reassessed poverty estimates in 11 Asian countries after taking into account household expenditures on health care. The impoverish-

ment approach has also been used in other fields of study such as housing affordability (Hancock, 1993; Kutty, 2005) and health insurance (Bundorf & Pauly, 2006).

The impoverishing effect of a medicine is defined in terms of the percentage of the population that would be pushed below an income level of US\$1.25 or US\$2 per day when having to purchase the medicine. Although different income levels have been used/proposed (Van Doorslaer et al., 2006; Chen & Ravallion, 2008), the US\$1.25 and US\$2 poverty lines were chosen because they are the most recent widely recognized poverty indicators as used by the World Bank (The World Bank Group, 2013b). Thus, the approach essentially compares households' daily per capita income before and after (the hypothetical) procurement of a medicine. If the pre-payment income is above the USD1.25 (or USD2) poverty line and the post-payment income falls below these lines, purchasing the medicine impoverishes people. We used this method to generate 'impoverishment rates', which denote the percentage of the population that would become impoverished. The unaffordability of a medicine then refers to the percentage of the population that either already is or would fall below the poverty line when having to procure the medicine. First, we consider the affordability of medicines in the total population at risk of becoming ill. We also indicate, using prevalence rates for the three chronic diseases, the expected number of patients actually affected.

## Data

To conduct the first analysis, three types of data were required per country: medicine prices, aggregate income data, and information on the income distribution. In calculating expected numbers of patients affected, prevalence data is also required. Medicine prices were taken from standardized surveys using the WHO/Health Action International (HAI) price measurement methodology, which report median patient prices for a selection of commonly-used medicines in the private sector, for both originator brand (OB) and lowest priced generic (LPG) products (Health Action International, 2012). We focused on the private sector because the availability of essential medicines in the public sector is much lower (Cameron et al., 2009b). In the countries studied here, therefore, many people will depend on the private sector for their medicines.

The World Bank's world development indicators (WDIs) provided household final consumption expenditure (HHFCE) data and information on income distribution (The World Bank Group, 2013c). Although WDIs have shortcomings (highlighted in the Discussion section), they have the advantage of being available for a wide range of countries. Moreover, in this context commonly used household surveys are often not available on a yearly basis and are not conducted in a standardized way, limiting the comparability of results across countries and over time (Van Doorslaer et al.,

2006; O'Donnell et al., 2008). This paper uses an affordability measure that can be quite easily applied in LICs and MICs where the use of more detailed household survey data may be limited.

HHFCE was selected as an aggregate income measure rather than GDP per capita as it better reflects households' resources (O'Donnell et al., 2008), while GDP also includes consumption, gross investment and net trade. Because the WDI did not provide any information on HHFCE for Nigeria and Yemen, the Economist Intelligence Unit (EIU) nominal private consumption figure was used for these countries (The Economist, 2013). For simplicity, we will refer to "income" as measured by HHFCE or nominal private consumption. Apart from average income, the WDIs also provide some information on a country's income distribution by listing the proportion of total income earned in seven income groups; five income quintiles, with the poorest and richest quintiles split into deciles.

At the time of analysis, medicine price surveys were available for 53 countries. In large countries such as India and China, price surveys were carried out on a state or provincial level (Cameron et al., 2009b). Because the WDIs do not provide state-level income distributions, HHFCE and population figures, these countries were excluded

**Table 1:** Overview of countries studied and years of data sources used.

Countries	Medicine price survey and WDI income data	WDI data on income distribution
<i>Low-income</i>		
Kyrgyzstan	2005	2003
Mali	2004	2001
Nigeria	2004*	2003
Pakistan	2004	2002
Tajikistan	2005	2004
Tanzania	2003	2000
Uganda	2004	2002
Uzbekistan	2004	2003
Yemen	2006*	2005
<i>Middle-income</i>		
El Salvador	2006	2002
Indonesia	2004	2002
Jordan	2004	2002
Mongolia	2004	2002
Peru	2005	2003
Philippines	2005	2003
Tunisia	2004	2000

\* Nominal private consumption from Economist Intelligence Unit was used.



from the current study. To ensure cross-country comparability, the analysis was limited to countries where income distributions (WDI data) were available from the year 2000 onwards. We used WDI income data from the same year as the WHO/HAI price data. Data on income distributions for the same year were used when possible, if not, the most recent income distribution data prior to the year of the price and income data were used.

Table 1 provides an overview of all countries and data used in this study. When discussing results, countries were grouped into LICs and MICs according to the 2008 World Bank's classification (The World Bank Group, 2013a). Sixteen countries were selected based on the availability of WHO/HAI data. They are not representative of the developing world as a whole. However, as these countries vary substantially in terms of economic development, health care infrastructure and medicine prices, they provide an interesting sample to study affordability of medicines.

We selected four medicines for which price data was available for the majority of countries and for which treatment regimens are relatively standard across countries. While these may not lead to results that are in a strict sense generalizable, they provide valuable insight in the affordability of common medicines in the selected countries. Table 2 lists the medicine, the ill health conditions for which these medicines are used, the total number of units per treatment course, and the treatment duration in days (Health Action International, 2012). Three of the four study medicines are used to treat chronic conditions (asthma, diabetes, and hypertension). For each of these, we also calculated the expected numbers of patients becoming impoverished, using the prevalence data shown in Table S1. We could not do this for Acute Respiratory Infection because of unavailability of comparable prevalence data.

**Table 2:** Description of studied medicines

Medicine name	Ill health condition	Medicine strength per dose	Total number of doses per treatment	Dosage form	Treatment duration in days
Salbutamol inhaler	Asthma	100 mcg	200	inhaler	30 (1 inhaler)
Glibenclamide	Diabetes	5 mg	60	capsule/tablet	30
Atenolol	Hypertension	50 mg	30	capsule/tablet	30
Amoxicillin	Acute Respiratory Infection	250 mg	21	capsule/tablet	7

The emphasis on medicines for chronic disease is justified by the fact that these conditions require ongoing, usually lifelong expenditures, making it more difficult for households to use financing strategies like borrowing and selling assets (Flores et al., 2008). Table 2 shows that the treatment duration for these medicines was

set at 30 days to represent the monthly treatment costs. The affordability of one acute condition (acute respiratory infection) treated with a 7-day treatment course of amoxicillin was also studied. Recently, the WHO increased the guidelines for treatment of acute respiratory infection with amoxicillin to a daily regimen of three times 500mg amoxicillin. This implies that the affordability of this medicine is likely to be lower than reported here (World Health Organization, 2008c).

### Calculation Methods

Our method to estimate the impoverishing effect of procuring medicines was based on the method as developed by Wagstaff and Van Doorslaer (2001; 2003) and explained by O'Donnell et al. (2008). However, using aggregate data requires some simplifying assumptions about the income distribution across population groups. For a detailed discussion of the method used to calculate the impoverishing effect of medicines, we refer to Niëns et al. (2009). The basic idea is to compare poverty estimates before and after a (potential) purchase of the medicines listed in Table 1. Average per capita income within each income group is estimated by combining information on the proportion of total income earned across income groups with data on the HHFCE (as provided by the WDIs). As only data on average income in the different quintiles and deciles was available, we assumed linearity of the income distribution within these relevant groups in which the USD1.25 and USD2 poverty lines were located in calculating poverty and impoverishment. The proportion of the population that would earn less than US\$1.25 or US\$2 per day after buying a medicine but not before would therefore be impoverished due to purchasing medicines. The medicine is deemed affordable for the proportion of the population that would remain above the poverty line after having purchased it. We also estimated the actual number of patients with one of the three chronic illnesses for which the medicine is unaffordable. To do so, we use prevalence rates from various data sources and again assume that the respective disease is evenly spread over the income distribution.

Because HHFCE is measured in current US\$, we recalculated the US\$1.25 and US\$2 poverty lines to US\$ values for the HAI/WHO survey year. HAI/WHO medicine prices were expressed in US\$ for the same year.

### 3.3 RESULTS

Table 3 presents the percentages of the population below the poverty line owing to the purchasing of each of the four study medicines, both LPG and OB products.

**Table 3:** Percentage of the population below the poverty line before procurement of the medicines and the percentage of the population below the poverty line after procurement of these medicines

Low-income countries		Salbutamol inhaler				Glibenclamide				Atenolol				Amoxicillin						
Country	GDP/cap (current US\$)	% of population below poverty lines and LPGW-wage, before medicine purchase				% of population below poverty line after medicine purchase				% of population below poverty line after medicine purchase				% of population below poverty line after medicine purchase						
		US\$1.25	US\$2	LPGW-wage	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	
Kyrgyzstan	478	0	14	10	8	5	22	18	*	2	*	2	*	1	*	15	*	12	*	26
Mali	422	37	61	85	51	50	67	69	66	53	76	65	*	*	*	*	*	*	*	*
Nigeria	639	56	77	90	71	*	77	*	71	71	79	79	67	63	83	81	79	68	80	84
Pakistan	644	-	8	46	0	*	13	*	0	0	13	12	1	0	17	12	4	4	21	21
Tajikistan	354	10	32	1	*	19	*	40	*	11	*	33	*	12	*	34	*	28	*	50
Tanzania	286	50	77	96	50	60	*	82	*	58	*	81	*	57	*	80	*	61	*	82
Uganda	305	52	73	90	59	54	77	74	*	53	*	74	72	53	85	74	74	54	86	74
Uzbekistan	365	17	38	68	28	24	50	46	*	22	*	43	*	19	*	41	*	35	*	58
Yemen	882	7	22	87	14	10	31	26	29	10	47	26	20	9	38	25	*	12	*	28
Middle-income countries		Salbutamol inhaler				Glibenclamide				Atenolol				Amoxicillin						
Country	GDP/cap (current US\$)	% of population below poverty lines and LPGW-wage, before medicine purchase				% of population below poverty line after medicine purchase				% of population below poverty line after medicine purchase				% of population below poverty line after medicine purchase						
		US\$1.25	US\$2	LPGW-wage	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB	LPG	OB
El Salvador	3067	7	11	59	9	9	14	14	17	11	21	16	15	12	19	17	21	*	26	*
Indonesia	1187	-	4	71	11	*	20	*	13	0	36	6	15	0	38	12	20	0	43	9
Jordan	2157	-	1	58	0	0	4	2	0	0	6	3	1	0	8	4	19	3	26	10
Mongolia	721	2	13	81	*	7	*	20	*	6	*	19	*	4	*	19	*	8	*	13
Peru	2852	2	9	64	7	5	14	11	*	5	*	11	13	4	20	10	27	7	33	14
Philippines	1156	5	21	88	16	12	32	28	23	13	38	29	27	12	41	28	23	17	37	32
Tunisia	2832	-	1	73	0	*	2	*	0	0	5	2	*	0	*	3	*	*	*	*

\* No reliable medicine price estimate was possible due to lack of data.

OB – Originator Brand LPG – Lowest Priced Generic

For each country, Table 3 first highlights the proportion of the population already below the US\$1.25 and US\$2 poverty lines without purchasing these medicines. These poverty estimates correlate highly with the commonly used (household survey based) estimates from the United Nations Development Program (UNDP) with Pearson correlation coefficients equal to 0.90 for the proportion of the population below the US\$1.25 poverty line, and 0.86 for the proportion below the US\$2 poverty line (United Nations Development Program, 2008). Table 3 also shows the proportion of the population earning less than the LPGW, which varies widely across countries: from only 1% in Tajikistan to 96% in Tanzania. This cross country variability represents one of the limitations of the LPGW-metric as used by the WHO/HAI methodology (World Health Organization & Health Action International, 2008).

Comparing the proportion of the population below the US\$1.25 and US\$2 poverty lines before and after procurement of medicines gives insight into the impoverishing effect of medicine procurement. By adding the proportion of the population already living below the US\$1.25 and US\$2 poverty lines to the group that would fall below these poverty lines when procuring the medicines, we get the proportion of the population for which the four medicines are unaffordable.

The results in Table 3 illustrate that the impoverishing effect of medicines varies substantially between OB and LPG products. For example in Yemen, a LIC where 7% of the population lives on a pre-payment income of less than US\$1.25 a day, OB glibenclamide purchased in the private sector would impoverish an additional 22% of the population versus 3% for the LPG equivalent. In Nigeria, a LIC where 56% of the population lives below US\$1.25 per day, purchasing amoxicillin from the private sector would impoverish an additional 23% if the OB is bought and 12% if buying the LPG.

Rather than showing proportions of the population, Table 4 presents both the absolute number of individuals that would be pushed into poverty due to the cost of buying medicines from the private sector ("Impoverished" column) and the number of people for which medicines are unaffordable ("Unaffordable" column). Besides absolute figures, in Table 5 we present the relative change of the poverty estimates for the total population studied as well as for the patient population. So, if 40% of the population is initially above the poverty line, while only 30% would remain above after purchasing medicines, this proportion is 25% (10% out of 40% are impoverished). These numbers are listed for all four medicines, both OB and LPG. The total population of the sixteen countries analyzed amounts to over 775 million people, of which approximately 126 million live on less than US\$1.25 and 209 million on less than US\$2 per day, respectively. Table 4 illustrates that across this set of 16 developing countries, for respectively almost one-fourth and two-fifth of the

**Table 4:** Absolute impoverishment and unaffordability estimates of medicines procured in the private sector for the total population across 16 countries (rounded down to millions)

Medicine	Total Population									
	Under USD1.25					Under USD2				
	Originator Brand	Unaffordable	Impoverished	Unaffordable	Lowest Priced Generic	Originator Brand	Unaffordable	Impoverished	Unaffordable	Lowest Priced Generic
Salbutamol inhaler	64	190	16	142	71	280	23	233		
Gilbenclamide	72	198	36	162	112	321	35	244		
Atenolol	79	205	20	146	133	343	50	259		
Amoxicillin	111	237	46	172	144	354	71	281		
	Chronic Patient Population									
Medicine	Under USD1.25					Under USD2				
	Originator Brand	Unaffordable	Impoverished	Unaffordable	Lowest Priced Generic	Originator Brand	Unaffordable	Impoverished	Unaffordable	Lowest Priced Generic
	Impoverished	Unaffordable	Impoverished	Unaffordable	Unaffordable	Impoverished	Unaffordable	Impoverished	Unaffordable	Unaffordable
Salbutamol inhaler	2,8	9,4	0,7	7,2	2,4	13,4	0,7	11,7		
Gilbenclamide	3,3	7,9	1,6	6,2	5,3	14,2	1,6	10,5		
Atenolol	19,4	58,3	6,6	44,4	29,3	92,4	10,3	73,4		

**Notes:**

The 'Impoverished column' shows the number of people that would be pushed below the USD 1.25 and USD2 poverty lines if the total population had to buy the respective medicine.

The 'Unaffordable column' shows the total number of people for which the respective medicine can be considered unaffordable.

total population essential medicines are unaffordable using the US\$1.25 and US\$2 poverty line.

The upper half of Table 4 shows the proportions of the total population for which medicines would be unaffordable when having to procure them. The actual number of people affected by this unaffordability (in terms of experiencing the disease) depends on the prevalence of diseases as well. Therefore, the lower half of Table 4 also shows the expected absolute number of patients affected by the unaffordability of medicines using the prevalence rates listed in Table S1 (Supplementary information). As the prevalence rates of hypertension are substantially higher than those of asthma and diabetes, the impoverishing effect, and therefore also the unaffordability, of atenolol is substantially higher than that for the other medicines. In this approach, given the height and distribution of income, impoverishment is determined by both medicine prices and prevalence rates for the relevant diseases.

**Table 5:** The relative change of the poverty estimates, i.e., the impoverished population expressed as a proportion of the population initially above the poverty line.

Total Population				
Medicine	additional percentage under USD1.25		additional percentage under USD2	
	<i>Originator Brand</i>	<i>Lowest Priced Generic</i>	<i>Originator Brand</i>	<i>Lowest Priced Generic</i>
Salbutamol inhaler	10	2	13	4
Glibenclamide	11	6	20	6
Atenolol	12	3	23	9
Amoxicillin	17	7	25	13
Chronic Patient Population				
Medicine	additional percentage under USD1.25		additional percentage under USD2	
	<i>Originator Brand</i>	<i>Lowest Priced Generic</i>	<i>Originator Brand</i>	<i>Lowest Priced Generic</i>
Salbutamol inhaler	10	2	10	3
Glibenclamide	10	5	18	5
Atenolol	12	4	21	7

### 3.4 DISCUSSION

The results illustrate that substantial proportions of the population would be pushed into poverty as a result of medicine procurement, implying that in many countries affordability of these treatments is low. In the private sector, LPGs were generally substantially more affordable than OB products. Thus, increasing the use of quality-assured generics could reduce the impoverishing effect of medicines. This use of

generics, in turn, could bring about improvements in the health status of these populations by avoiding low compliance to recommended dosages or duration of treatment, resulting in problems such as sustained hypertension, elevated blood glucose levels, or the promotion of bacterial resistance due to too short courses of antibiotics.

Our calculation method has the advantage of allowing for comparisons of medicine induced impoverishment across time and across countries using widely available aggregate data. The method, therefore, is useful and generalizable to study the affordability of a wide range of goods and health care services. The use of such data also brings some limitations, which are discussed in further detail in Niëns et al. (2009). First, dividing HHFCE by total population to get an estimate of income per capita assumes that each household is the same size. However, poor households are generally larger than their richer counterparts (Lipton & Ravallion, 1994). This discrepancy causes the average income per capita to be overestimated in the lower income groups, making our affordability estimates rather conservative. Second, the assumption of linearity of the income distribution between income groups is also likely to lead to an overestimation of average incomes across the income distribution and therefore to a downward bias in our results. We also assumed a linear distribution of illness over the income distribution to calculate expected numbers of affected people. Although, in general, disease may be more prevalent in low-income groups, which would imply conservative estimates of unaffordability, this also depends on the exact diseases studied. Moreover, it is clear that considering only medicine costs, for four medicines independently, merely demonstrates the larger problem of medicine and health care affordability. The treatment of chronic conditions often requires a combination of medicines and is therefore likely to be even more unaffordable than what is reported here (Cameron et al., 2009b). For chronic asthma patients, for example, appropriate management of their disease requires use of both salbutamol and beclometasone inhalers for treatment and prevention (Health Action International, 2012). Due to the lack of available price information on beclometasone inhalers (because of poor availability), it was not possible to include this medicine in the analysis. As such, the true affordability of asthma treatment is likely to be lower than reported in Table 3 and 4. Having said this, the medicines studied in this paper are commonly used to treat ill health conditions from which considerable proportions of the population in the developing world suffer, as is also illustrated in Table S1 (World Health Organization, 2004a). As such, low affordability of these medicines is likely to signal a more general problem of low affordability of medicines in LIC and MIC. Further, it should be noted that comparability of impoverishment rates for acute and chronic conditions may be limited. If people suffer from an acute respiratory infection, on average, three times per year and are able to shift resources over time, the impoverishment rates for amoxicillin should be interpreted

with caution. Further research is needed on this issue, for example by calculating affordability for standardized time periods taking into account the relevant incidence rates of respiratory infections.

Notwithstanding these limitations, this study provides useful insights into the affordability of these four medicines in the developing world. When medicine prices are known, the methods used, as they rely on easily obtainable aggregated data, can be used to compare affordability of medicines across countries and over time. Clearly, medicines represent only a part of the costs associated with the management of an illness. Other costs, such as for diagnostics, physician consultations and transport costs to clinics, lost work time etc., place an additional burden on household finances in developing countries. However, given the relatively large share of health care costs for medicines in developing countries (World Health Organization, 2000; World Health Organization, 2004b; Van Doorslaer et al., 2006; Cameron et al., 2009b), medicine affordability is likely to be an important determinant to access to treatment.

This study shows high medicine costs can push large groups of patients into poverty. These results call for action, both by governments, civil society organizations and others, to make access to essential medicines a priority, and not only to ensure access to necessary medicines, but also in the context of reducing poverty. Possible lines of action include developing, implementing and enforcing sound national and international price policies. In the short term these policies could encompass, for example, restrictions on supply chain mark-ups, tax exemptions and regulating prices for end-users. Promoting the use of quality assured, low-cost generics, for example through preferential registration procedures, is also an important strategy (Cameron et al., 2009b). In the public sector, ensuring availability of essential medicines at little or no charge to the poor is critical. In the longer-term, establishing health insurance systems with outpatient medicine benefits, seems crucial to avoid poverty due to health shocks (and poor health due to poverty). Innovative approaches, such as using private distribution systems to supply subsidized medicines to chronic disease patients, should also be considered. For medicines which are still subject to patent restrictions, pharmaceutical companies should be encouraged to differentially price these products as occurs with antiretrovirals (Waning et al., 2009). Countries also have the option to use compulsory licensing to oblige patent holders to grant its use to the state or others (World Health Organization, 2006), as was recently done by Thailand (Ford et al., 2007; Seim, 2007).

When resources are limited, those in greatest need, such as people suffering from chronic disease who earn less than US\$1.25 per day, should benefit from state and/or donor actions. The price in terms of health losses due to unaffordable medicines is something we cannot afford.



## SUPPLEMENTARY INFORMATION

**Table S1:** the prevalence of three chronic diseases

Condition	Proportion of the population suffering from		
	asthma	diabetes	hypertension
<i>Low-income</i>			
Kyrgyzstan	4,3	4,3	28,0
Mali	2,6	3,3	27,5
Nigeria	5,7	3,9	34,8
Pakistan	4,1	7,6	24,0
Tajikistan	4,3	1,0	24,0
Tanzania	4,4	2,6	27,5
Uganda	4,4	1,7	27,5
Uzbekistan	4,3	7,0	7,6
Yemen	5,8	2,5	9,7
<i>Middle-income</i>			
El Salvador	3,8	7,8	42,0
Indonesia	3,3	4,6	23,3
Jordan	5,8	7,5	22,2
Mongolia	2,1	1,3	42,0
Peru	9,9	5,6	15,2
Philippines	7,9	6,7	20,2
Tunisia	3,7	8,5	33,0

Diabetes prevalence data was retrieved from the international diabetes federation's data website (<http://www.diabetesatlas.org/>).

Asthma prevalence comes from the Global Initiative for Asthma's Burden of Asthma Report (<http://www.ginasthma.com/ReportItem.asp?l1=2&l2=2&intId=94>).

Hypertension prevalence comes from WHO infobase online (<https://apps.who.int/infobase/report.aspx>) and a Lancet article by Kearney et al. (2005).

# Chapter 4

## Measuring the Affordability of Medicines: Importance and Challenges

Published as:

Niëns LM, Brouwer WBF. "Measuring the affordability of medicines:  
Importance and challenges"

*Health Policy* 2013 112(1): 45-52.



**ABSTRACT**

The issue of affordability of health care services remains high on the (health) policy agenda. Determining whether health care services are affordable is complex however, as the concept 'affordability' is inherently normative. With a focus on measuring affordability in low- and middle-income countries, we discuss different methods used to operationalize this concept. Using the example of medicine purchases in Indonesia, we show the choice of method and threshold to have a significant impact on outcomes. We argue it is important to further standardize methods and appropriate threshold use in applied research to increase comparability of results and to facilitate sound assessments of affordability.

## 4.1 INTRODUCTION

Issues of affordability appear to be at the center of health care discussions and decisions. Politicians and health care policy makers alike, in high- and low- and middle-income countries (LMICs), see themselves confronted with the challenge of ensuring and, where possible, increasing access to health care services of sufficient quality for all those in need while at the same time containing (public) health care expenditures. This challenge raises numerous important questions and dilemmas. Some have even argued that these goals form an 'inconsistent triad', i.e., that they can never be completely fulfilled simultaneously (Weale, 1998). Still, policy makers may attempt to strike an optimal balance in reaching these goals.

An important issue in that context is that of affordability. In both high as well as low- and middle-income countries policy makers struggle with questions regarding the payments people should be able to make out-of-pocket (OOP) on health care or through copayments in some form (affordability at micro level) and the sustainability of public funding of the health care sector raised through premiums or taxes (affordability at macro level) (Van Doorslaer et al., 2006; Cameron et al., 2009b). Because in LMICs the large majority of the population does not have health insurance (Dror et al., 2002), OOP payments are an important source of health care financing. Much of these OOP payments are on medicines, as in LMICs medicine expenditures often constitute a large portion of total health expenditures (World Health Organization, 2000; World Health Organization, 2004b; Van Doorslaer et al., 2006; Cameron et al., 2009b; Niëns et al., 2010). Indeed, as in LMICs the availability of 'free' quality assured medicines in the public sector often is low, people are forced to buy their medication in the private sector where prices are commonly high (Cameron et al., 2009b). This immediately stresses the issue of affordability. By definition, an average individual in a low- or middle-income country has only a limited amount of resources with which all basic needs (food, housing, etc.) need to be fulfilled. The amount of money people thus can spend on health care, or more specifically medicines, therefore is limited. If prices of these medicines exceed the budget, people may forego procurement of essential drugs, go into debt or forego other essential purchases (Flores et al., 2008; Cameron et al., 2009b; Niëns et al., 2010). This stresses the gravity of the topic of affordability, which is also emphasized in several international treaties in which the access to health care is established as a right. This therefore must imply that OOP payments should be, somehow, 'affordable' (United Nations General Assembly, 1948).

In this paper, we will highlight the issue of defining and measuring affordability. We focus on affordability of health care, and medicines in particular, at the micro level in LMICs. We will emphasize how different methods to quantify affordability

can have their specific limitations and lead to different results. Within methods, a further source of variation in affordability is setting a specific threshold for affordability. We will address these issues generally and will use the example of Indonesia to illustrate our point.

The paper is structured as follows. After a concise introduction of affordability, we first discuss several empirical studies of affordability in health care. We will highlight the differences in methods used and differences in operationalizations of similar methods. Next, we use an example of hypothetical medicine procurements in Indonesia to show how these different methods and their operationalizations influence the outcome of affordability measurement. The paper concludes by arguing that further standardization of methods used in this area will allow better comparison of results across studies and may stimulate further debate on when specific health care interventions can be deemed affordable or should be deemed unaffordable.

## 4.2 ON AFFORDABILITY OF HEALTH CARE AND MEDICINES

Affordability is an important, yet hard to define let alone operationalize concept. This has much to do with the fact that, by definition, defining affordability is a normative issue (Bradley, 2008). Indeed, it requires defining when we consider something to be too expensive for someone. One (extreme) answer could be that a good is unaffordable when the price of that good/service exceeds the total budget a person can attract. That however disregards all other spending (even at subsistence level) that a person needs to do. Another viewpoint could be that a person should at least be able to fulfill other basic needs after having purchased the good/service. From such a viewpoint a good is unaffordable if the individual, after the purchase, does not have enough resources left to fulfill his basic needs, i.e., falls below a poverty line. A difficult subsequent issue relates to the level at which the poverty line is set. A final alternative would be to link the price of a good/service to the income of the individual and require it not to exceed some percentage of total income. Again here, a difficult next question is what this percentage should be exactly. When is it too expensive, that is, unaffordable? Unsurprisingly therefore, scholars in various fields, working on defining and measuring affordability, have indeed acknowledged the normativity of the affordability concept (Whitehead, 1991; Komives et al., 2005; Milne, 2006; Stone, 2006; Bradley, 2008; Niëns & Brouwer, 2009; Niëns et al., 2012). Moreover, it need not surprise that in applied work different concepts are used to calculate affordability in different areas such as housing (Hulchanski, 1995; Kutty, 2005; Stone, 2006), education (Usher & Cervenán, 2005; Murakami & Blom, 2008),

transportation (Carruthers et al., 2005; The World Bank Group, 2007) and utilities (Frankhauser & Tepic, 2005; Milne, 2006).

In many studies investigating (un)affordability of goods and services, the focus is on estimating a proportion of the population for which a particular good or service is unaffordable. In general, this requires three different sources of information: i) the price of a commodity or service; ii) income(s), and iii) some measure of unacceptable burden (Hancock, 1993; Niëns et al., 2012). The latter shall be labeled as 'threshold' henceforth. Whereas the first two parameters are to a large extent a matter of obtaining appropriate data (which can be challenging as well), setting the threshold essentially involves a normative choice, but one that influences the outcomes significantly. It thus lies at the heart of the 'vagueness' (Bradley, 2008) of the affordability concept and appears an issue that deserves more debate and, if possible, further standardization.

In calculating affordability, the two most applied methodologies relate to the concepts of impoverishment and catastrophic spending as developed and applied by renowned health economists (Wagstaff & Van Doorslaer, 2001; Wagstaff & Van Doorslaer, 2003). Methods based on the impoverishment concept calculate the proportion of the population that, after spending on a good/service, drops below a *relevant poverty line*. Thus, the impoverishment method works from the premise that there is an absolute minimum level of income people require for basic necessities. Implicitly, some poverty line is used as a threshold, therefore. The other method, catastrophic payment, calculates the proportion of the population that would spend more than X percent of their income to pay for a good/service. This method thus sets a threshold in terms of a forgone *proportion of income*. The underlying idea is that if a household spends a larger fraction of its income than the specified percentage on a particular good or service, it will have to scale back its consumption in other areas to an inappropriate extent. A common way of using these methods is to retrospectively assess how many people actually experienced impoverishment or catastrophic payments due to expenditures (on health care) (Wagstaff & Van Doorslaer, 2001; Wagstaff & Van Doorslaer, 2003). The methods can also be used to prospectively calculate the proportion of the population for which the good *would be* unaffordable if it needed to be purchased. This provides insight in the proportion of the population at risk of facing either impoverishment or catastrophic payments *if the good or service would need to be bought* (Niëns et al., 2010).

Because affordability in the impoverishment and catastrophic payment methods is calculated in relation to the actual incomes in the population, they automatically take into account the income distribution. An alternative methodology recently developed by the World Health Organization (WHO) and Health Action International (HAI) measuring affordability does not use this distribution. This straightforward

method expresses the affordability of medicines in the number of days' wages the lowest paid unskilled government worker (LPGW) needs to spend to procure a course of treatment of a particular medicine (World Health Organization & Health Action International, 2008; Cameron et al., 2009b). WHO/HAI do not pose a threshold with the LPGW-method and leave the judgment regarding whether some medicine is deemed affordable to local policy makers who more easily can position the LPGW wage in relation to the average income (and its distribution) of the local population. Each of these three methods has own limitations, which will be briefly discussed in the next section.

### **Different methods, different limitations**

The retrospective or prospective application of the impoverishment method captures the people that were or would be pushed below some relevant poverty line due to the procurement of health care or medicines (the impoverishment rate) and, as such, immediately shows which proportion of the population was impoverished or is potentially at risk of becoming impoverished. The method's main weakness is that it normally works from a rather extreme threshold. If used naively the method also ignores those already below the poverty line, which obviously can be easily corrected by including those living below that line anyhow (Niëns et al., 2010). Furthermore, for those people who are not pushed below a (commonly low) poverty line, but nonetheless experience a strong income drop, the relevant good is not deemed unaffordable, which may be considered debatable. Elevating the poverty line to a higher level could help, of course, but at the same time stretches the concept of poverty. A clear consensus on what the poverty line is or should be, does not exist. This is reflected in the range of values used in applied literature (Xu et al., 2003; Van Doorslaer et al., 2006; Limwattananon et al., 2007; Somkotra & Lagrada, 2008; Cameron et al., 2009b; Sun et al., 2009; Niëns et al., 2010). Hence, the more fundamental question is what poverty actually entails.

The main weakness of the catastrophic payment approach is that the rich, who can easily spend more than X percent of their income on medicines without suffering any hardship, are included in the estimates of 'unaffordability', while the very poor, for whom spending less than X percent may already be difficult (due to strict budget constraints and perhaps being pushed under a poverty line) are not. Hence, the method may not fully capture those individuals in estimating affordability, for which affordability, loosely defined, is actually a problem. The main question remaining in the catastrophic payment approach hence concerns the level of spending to be deemed affordable, and whether such a level might differ for high and low incomes.

The main advantage of the LPGW method is its simplicity and straightforwardness, both in terms of its application and how, on a local level, many people may be able to position themselves in relation to this LPGW. However, in its simplicity also lies its main weakness, i.e., knowing the number of daily wages the LPGW needs to pay for a course of medicines does not provide clear information on what this means for the population as a whole. Furthermore, its link to the concept of affordability also is less clear as is setting a threshold for the number of days the LPGW needs to work for medicines.

A shortcoming the three methods have in common is that comparing their results across countries and time is not possible when different thresholds (let alone methods) are used. The choice of methods and their operationalization thus requires attention. This is highlighted in the next section, where we focus on the most commonly used impoverishment and catastrophic payment methods.

### **Practical applications of the methods**

As the impoverishment and catastrophic payment methods define affordability in different ways, they can yield different answers to the question whether some medicine is affordable to specific populations. Moreover, *within* methods the variation in answers can also be rather large when different poverty lines are used within the impoverishment method or when different percentages are used in operationalizing the catastrophic payment method. The next paragraph will substantiate this point by summarizing the findings of different empirical studies (it needs noting that different data sources can also affect the outcomes).

Several studies have been conducted applying these methods in the health care sector. In investigating the effect of OOP payments in health care on poverty estimates in 11 LMIC, Van Doorslaer and colleagues used the World Bank's absolute PLs of US\$1.08 and US\$2.15. Using household data and actual expenditures they retrospectively show 78 million people to have dropped below the US\$1.08 poverty line when their payments for health care were subtracted from their incomes (Van Doorslaer et al., 2006). Niëns et al. (2010) worked with the World Bank's 2005 poverty line of US\$1.25 and US\$2.00 (The World Bank Group, 2008) to calculate medicine affordability for four essential medicines across 16 LMICs with a total population over 775 million. Applying the methods prospectively, their results for example indicate that, at the US\$1.25 PL, the lowest cost medicine (salbutamol inhaler), would be unaffordable for 140 million people in these countries (Niëns et al., 2010). Finally, in Mexico, Knaul et al. (2006) applied a US\$1.00 threshold, reporting 3.8% of families to suffer from impoverishing health care expenditures each trimester.



Besides these PLs other thresholds have been used as well within the impoverishment method. In Vietnam, Wagstaff and Van Doorslaer applied both a food-based PL, based on the cost of reaching an intake of 2100 calories per day, as well as a poverty line that captured spending requirements on food and non-food items (Wagstaff & Van Doorslaer, 2003). Furthermore, in Thailand several studies used the official national poverty line adapted to the specific province (Limwattananon et al., 2007; Somkotra & Lagrada, 2008). These studies showed that households using private inpatient services had a higher incidence of impoverishment (Limwattananon et al., 2007) and that impoverishment rates decreased after the implementation of a policy broadening insurance coverage (Somkotra & Lagrada, 2008).

For catastrophic payment methods in the realm of health care, Xu et al. (2003) retrospectively applied a threshold of “40% of income remaining after subsistence needs have been met”. They found that a 1% increase in the total proportion of total health expenditures provided by out-of-pocket payments resulted in a 2.2% increase in households facing catastrophic payments. Although Sun et al. (2009) also used the 40% of non-food expenditure threshold when retrospectively calculating the affordability of total health care in rural China, using sensitivity analyses with thresholds of 20%, 30%, 50% and 60%, they found catastrophic payments to decrease by 34.77% comparing the 20% and 60% thresholds. Using similar thresholds (20%, 30%, 40% and 60%) in a study in Burkina Faso, Su et al. (2006) found catastrophic health care payments to decrease by 57.26% comparing the 20% and 60% thresholds. Niëns et al. (2012) prospectively applied a 5% threshold of daily income when calculating the affordability of an anti-diabetic drug, glibenclamide, and found 65.9% and 78.6% of the Indonesian and Indian populations respectively to be at risk of facing catastrophic payments. Wagstaff and Van Doorslaer (2003) retrospectively used a range of thresholds (2.5%, 5%, 10% and 15%) which were applied for both pre-payment income and non-food expenditures. One of their findings was that, in Vietnam, it was not inpatient care that increased poverty so much, but rather expenditures related to non-hospital care like medicine procurements. Knaul et al. (2006) also applied the catastrophic payment method but did so using a 30% threshold of income. Whereas they found almost all households with impoverishing effects to be from the poorest quintile, catastrophic health care payments were observed throughout the income distribution. In Thailand, whereas Limwattananon et al. (2007) applied a threshold of 10% of total consumption including expenditures on food Somkotra and Lagrada (2008) used ranges of thresholds of both total consumption (5%, 10% and 15%) and non-food consumption (20%, 25% and 30%). Both studies reported that moving towards implementation of universal health insurance coverage in 2001 decreased catastrophic payments (Limwattananon et al., 2007; Somkotra & Lagrada, 2008).

The previous overview shows the affordability of health care and medicines in LMICs to vary and highlights the different thresholds used between, but also within methods. Whereas some of these differences are likely to be data driven others may reflect differences in approach to, or (even) opinion about, affordability.

Using the LPGW methodology, Cameron et al. (2009b) find medicine affordability to differ significantly between WHO-regions. They show that, whereas treating an ulcer with a month's course of private sector OB ranitidine (150 mg capsules or tablets, two a day for 30 days) costs more than 35 days' wages in Africa, in Southeast Asia this is just 2.7 days' wages. Moreover, when defining affordability in relation to some normative threshold in terms of a maximum number of wage days a person could spend on a purchase of medicines before deeming it unaffordable, similar problems regarding comparability between studies could occur as for the two other methods described above. These results are summarized in Table 1.

We will show that the previously explained differences and choices are not only theoretical but in effect influence outcomes. To illustrate this, and to stimulate the debate regarding appropriate and comparable measurement of affordability, we prospectively calculate the affordability of Lowest Priced Generic (LPG) glibenclamide, amoxicillin and atenolol in Indonesia, using both the impoverishment and catastrophic payment methods.

### 4.3 PUTTING THE METHODS INTO PRACTICE: THE CASE OF MEDICINE AFFORDABILITY IN INDONESIA

Niëns et al. (2012) used LPG prices to prospectively calculate the affordability of LPG glibenclamide (used for treating diabetes; 5mg per tablet at a daily cost of US\$0.11) in Indonesia. They applied the impoverishment method as described by O'Donnell et al. (2008), using household level income data from the 2005 wave of the Indonesian National Socioeconomic Survey (Susenas – n=7302 households) (RAND Corporation, 2011). Thus, they calculated the percentage of the population that would be pushed below a poverty line when having to procure LPG glibenclamide. Using PLs of US\$1.25 and US\$2.00 they found 28.8% and 61.7% of the population, respectively, to already live below the poverty line *before* hypothetical medicine purchases. For them, the medicines may therefore be deemed unaffordable *at any price* above zero.

Applying the impoverishment method prospectively indicated that 5.8% and 3.7% of the population would be impoverished due to medicine procurement, using the two respective poverty lines (Niëns et al., 2012). Working with the prospective catastrophic payment method and a threshold of 5% (using household level income

Table 1: Affordability studies in Health care

Authors	Country	Topic	Method: Impov. / Cat.	Income measure	Poverty Line used	Results
Van Doorslaer et al. (2006)	11 LMICs.	Total healthcare costs	Impov. (R)	HH-surveys.	- US\$1.08 & US\$2.15.	78 million people dropped below US\$1.08 due to HC costs.
Niëns et al. (2010)	16 LMICs.	Medicine affordability	Impov. (P)	Estimates from aggregated World Bank data.	- US\$1.25 & US\$2.00.	At US\$1.25 salbutamol inhaler is unaffordable for 140mln. people on pop. of 775 mln.
Knaul et al. (2006)	Mexico.	Total healthcare costs	Impov. & Cat. (R)	Mexican Survey of HH income and exp.	- US\$1.00 - 30% of total income minus food exp.	3.8% of pop. impoverished (most in low-income quintiles) / cat. payments over total income distribution.
Wagstaff and Van Doorslaer (2003)	Vietnam.		Impov. & Cat. (R)	Total HH cons., gross of OOP payment for health services.	- Food poverty line (FPL) based on cost of reaching 2100 calories per day - Poverty line capturing spending on food and non-food items.	Between '93 – '98: - Impov. FPL ↓ from 4.4% to 3.4%. For the poverty line impov. increased: 0.4% to 0.5% - Cat. payments more concentrated amongst the poor but ↓ in time period.
Limwattananon et al. (2007)	Thailand.	Total healthcare costs	Impov. & Cat. (R)	Total HH- exp.	- Official national poverty line adapted to regions - 10% of total cons.; food included.	Cat. payments mostly occur for inpatient services (31.0% in '00 and 14.6% in '04). For outpatient services they ↓ by approx. 33% (12.0% in '00 to 8.3% in '04).
Somkotra et al. (2008)	Thailand.	Total healthcare costs	Impov. & Cat. (R)	Total HH-cons.	- Province-specific PL. - 5%/10%/15% of total cons. - 25%/30% of non-food cons.	Introduction UC in '00: Cat. payments ↓ by 24.48% between '00 – '04. Impov. Decreased from 1.23% to 0.58% in same time period.

Authors	Country	Topic	Method: Impov. / Cat.	Income measure	Poverty Line used	Results
Xu et al. (2003)	59 countries.		Cat. (R)	HH-surveys.	- 40% of income minus average food exp.	1% ↑ in proportion total HC exp. Paid for by OOP payments à 2.2% increase in HHs facing cat. Payments.
Sun et al. (2009)	Rural China; Shandong Province.	Total healthcare costs.	Cat. (R)	HH-survey.	- 40% of income minus average food exp.; with sensitivity analysis of 20%-30%-50% -60%	Cat. payments decreased by 34.77% between 20% and 60% thresholds.
Su et al. (2006)	Burkina Faso.	Total healthcare costs.	Cat. (R)			Cat. payments ↓ by 57.26% between 20% - 60% thresholds.
Niëns et al. (2012)	Indonesia and India.	affordability glibenclamide (anti-diabetic)	Cat. (P)	HH- surveys.	- 5% threshold of daily income.	65.9% of Indonesian & 78.6% of Indian pop. face Cat. payment
Cameron et al. (2009b)	36 countries.	Medicine affordability	LPGW (P)	N/A.	N/A.	Affordability differs much in WHO-regions.

Cat.: catastrophic – cons.: consumption – exp.: expenditure – FPL: food-poverty line – HC: health care – HH: Household – Impov.: Impoverishment – LPGW – Lowest Paid Government Worker – N/A: not applicable – OOP: out-of-pocket – PL: poverty line – pop.: population – UC: universal coverage – (P): prospective – (R): Retrospective ↓: decreased – ↑: increased.

data), indicated that a proportion of 65.9% of the population would not be able to purchase glibenclamide without a catastrophic payment exceeding 5% of their daily income (Niëns et al., 2012). Using the LPGW approach WHO/HAI finds the LPGW needs 0.6 days' wages to pay for one course of treatment.

Here we repeated the same calculations for glibenclamide, amoxicillin (used for treating an acute respiratory infection; 250mg per tablet at a daily cost of US\$0.27) and atenolol (against hypertension; 50mg per tablet at a daily cost of US\$0.43) (see Table 2: panel A).

**Table 2:** Affordability estimates: impact of methods and thresholds

**Panel A:** Affordability estimates for 3 LPG medicines with micro data and methods

Methods	Outcome measure	Medicine (condition)		
		Glibenclamide (diabetes)	Amoxicillin (acute respiratory infection)	Atenolol (hypertension)
Impoverishment	impoverishment rate <US\$1.25 PL	5.8%	14.2%	21.6%
	impoverishment rate <US\$2.00 PL	3.7%	8.2%	11.6%
Catastrophic payment	Catastrophic payment at 5%	65.9%	95.8%	98.6%
Lowest paid government worker	# of daily wages needed	0.6 days	0.4 days	2.4 days
<b>Panel B:</b> Impoverishment rates at different thresholds				
	2011 National PL Indonesia (US\$0.89)	4.7%	13.5%	22.5%
	US\$1.08	6.0%	15.2%	23.5%
	US\$2.15	2.8%	6.3%	9.3%
<b>Panel C:</b> Catastrophic payments at different thresholds				
	1.0%	>99%	>99%	>99%
	2.5%	92.3%	>99%	>99%
	5.0%	65.9%	95.8%	98.6%
	7.5%	37.1%	88.1%	96.4%
	10.0%	17.2%	78.0%	92.5%

Besides the US\$1.25 and US\$2.00 PLs, we used the same household level income data to calculate the impoverishment and catastrophic payment rates for these three medicines at different thresholds. Impoverishment rates were calculated for the US\$1.08 and US\$2.15 PLs as used by Van Doorslaer et al. (2006) and the 2011 national poverty line of Indonesia which is US\$0.89 (The Economist, 2012). All calculations

were done with PLs that were recalculated to local currency units using the Purchasing Power Parity conversion factor from 2005 (The World Bank Group, 2011b). Panel B shows the impoverishment rates to vary strongly with the thresholds used. Whereas for glibenclamide we find 4.7% of the Indonesian population impoverished at the national poverty line, for the US\$1.08 and US\$2.15 this is 6.0% and 2.8% respectively. For amoxicillin and atenolol these proportions range from 15.2% and 23.5% at the US\$1.08 poverty line to 6.3% and 9.3% at the US\$2.15 PL, with the impoverishment rates at Indonesia's national poverty line, i.e., 13.5% for amoxicillin and 22.5% for atenolol falling in between.

Varying the catastrophic payment thresholds we also find large differences (see Panel C). If people are allowed to spend no more than 1.0% of their daily income on glibenclamide this medicine is unaffordable for more than 99% of the population, whereas increasing the threshold to 10% results in glibenclamide being deemed unaffordable for 17.2% of the population. For amoxicillin and atenolol these proportions range from over 99% for the 1% threshold to 78% and 92.5% at the 10% threshold, respectively.

#### 4.4 CONCLUSION AND DISCUSSION

Affordability is an important issue in many health care systems, especially those in LMIC. Van Doorslaer et al. (2006) highlight that only in Asia, already 78 million people would be pushed below the poverty line of \$1 per day after paying for health care. Medicines commonly constitute a large part of health care consumption. In many LMICs countries, therefore, essential medicines are unaffordable for many (Cameron et al., 2009b; Niëns et al., 2010). Niëns et al. (2010), for example, estimated that for over two-fifths of the in total approximately 775 million people in 16 LMICs, essential medicines are unaffordable. They show this problem to be especially pressing for people suffering from chronic non-communicable diseases which require life-long ongoing medicine purchases (Niëns et al., 2010).

These figures demonstrate that improving the affordability of health care, and especially medicines, should be an important policy goal. The current levels of unaffordability can have important detrimental health effects in the most vulnerable groups in the world. Governments have several options at their disposal to increase the affordability of health care and medicines, also in LMICs. From ensuring that quality assured generic medicines are available in the public sector, to removing import levies on medicines and exempting them from value added tax, to implementing regulated (regressive) mark-up systems for medicines in the distribution chain (Cameron et al., 2009b). Furthermore, installing pre-payment schemes (insurance) to

finance healthcare offers the possibility for governments to better control (generic) medicine purchases and prices (Lee et al., 2006; Boonen et al., 2010; Dylst et al., 2011). Such policies are ideally based on sound information on the current problem and evaluated to judge their impact. In that context it is pivotal to measure and quantify affordability.

Over the years, useful methodology has been developed by leading experts in the field that allows the quantification of the inherently 'vague' concept of affordability (e.g. Wagstaff & Van Doorslaer, 2001; Wagstaff & Van Doorslaer, 2003). Still, as the literature and our results show, the impact of the methods chosen to measure affordability as well as the thresholds chosen within those methods is significant on final outcomes. It appears that the observed differences, which are also reflected in the empirical literature regarding affordability, reflect the difficulty of univocally grasping the concept of affordability and to find suitable and general thresholds for affordability. The two most prominent methods, the impoverishment and the catastrophic payment method, both use different operationalizations of the concept of affordability and within the methods different thresholds are used, reflecting the difficulty in setting one unique standard for affordability. While the difficulty is understandable, the implications are worrisome since arbitrary variations in thresholds may strongly affect affordability estimates and, hence, may –unduly if the thresholds or methods may be deemed inappropriate– influence policy makers and the sense of urgency regarding matters of financial access to health care and medicines.

In light of these findings, we argue that two things would be useful. First, it may be worthwhile to create a (preliminary) standard for calculating affordability. Rather than attempting to develop new methods (with own limitations) a fruitful way forward is to work with a fixed combination of methods and a fixed combination of affordability thresholds. As a first suggestion, we would recommend using both the impoverishment and catastrophic payment methods. This would ensure that large proportions of income being spent or required for the purchase of medicines would be detected (even when these do not push the individuals involved into poverty) and that those individuals who are pushed into poverty would also be detected; even when the proportion of income spent on medicines is fairly limited. Second, in terms of a threshold, it seems that a general discussion between policy makers and researchers leading to a (standard) range of thresholds would be a logical choice, given the current variation.

We emphasize that the threshold can and should be set in relation to the good or service under study. For instance, since medicines form only a portion of total health care expenditures, one may set catastrophic payments thresholds and impoverishment thresholds higher/lower when studying medicine expenditures than

when studying health care expenditures. Studying partial expenditures in some area should be judged against different thresholds than when considering the whole. Similarly, a distinction could be made between chronic and acute diseases, as the former require ongoing, sometimes lifelong expenditures. These may, *ceteris paribus*, sooner be considered unaffordable than once only purchases. For instance, in case of chronic conditions, it is less possible for people to use coping mechanisms like spending savings, loaning or selling assets to pay for the health care expenditures (Flores et al., 2008).

To help politicians and governments improve the access to medicines, we therefore argue scholars and policy makers should discuss and agree on an international benchmark for how to best address the affordability question. An international benchmark, both in calculating and reporting, would foster transparency and inter-temporal and international comparison. Since comparison in itself can increase the awareness and sense of urgency for governments to act swiftly on these issues, such a benchmark should be discussed.

To conclude, affordability is important and increasingly quantified. In order to increase comparability, also across countries, we urge for a further standardization of the measurement of affordability.





# PART II

Affordability at the Macro Level in a  
Developed Country: Delineating Entitlements  
in (social) Health Insurance Systems





# Chapter 5

## Delineating the Benefit Package: The Necessity of Insurance Criterion in the Netherlands

*Submitted Article*



## ABSTRACT

In the Netherlands, the Dutch Health Care Insurance Board (CVZ) is responsible for managing the basic benefit package. In the last two decades, CVZ has developed a framework, combining four criteria (necessity, effectiveness, cost-effectiveness and feasibility), to inform reimbursement decisions. Although, in general, there is consensus about these criteria, not all aspects of the criteria are sufficiently operationalized, which frustrates their application. One issue currently receiving much attention is that of affordability in the context of necessary to insure interventions. CVZ tries to cover this issue with a 'necessity of insurance' criterion which is part of the Necessity criterion. At present it is relatively unclear what this sub-criterion exactly entails and how it could be used in a systematic way in package management. Here we take forward this criterion's operationalization by introducing a checklist that allows its application to be systematic, both in terms of content as well as process.

## 5.1 INTRODUCTION

Over the last decades health care costs have increased rapidly (Meltzer, 2001; Folland et al., 2004). This has raised a number of issues. First, governments may feel the need to justify the increasing expenditures on health care, also in light of the often mandatory nature of the contributions. This may involve demonstrating that the resources are spent on technologies that offer value for money. Second, the financial sustainability and affordability of the health care system may become a matter of debate. This calls for measures allowing the control of expenditures, also to ensure the accessibility of highly important facilities to future citizens. In order to control expenditures, many countries with (social) health care insurance schemes have taken various measures, like implementing deductibles and co-payment arrangements (Schoen et al., 2010; Barros et al., 2011; Organization for Economic Co-operation and Development, 2012). Another important development is that the content of basic benefit packages (the entitlements of the socially insured) is more frequently critically examined (Schreyogg et al., 2005; le Polain et al., 2010). This may be illustrated by the use of Health Technology Assessment in an increasing number of countries (Franken et al., 2012; Kolasa & Wasiak, 2012). By clearly delineating the basic benefits package, through selectively taking out interventions or restricting entry of new interventions, health care expenditures can be controlled, but increases in expenditures can also be justified. However, this requires clear and broadly supported criteria for how to delineate the basic benefits package.

In the Netherlands, the Dutch Health Care Insurance Board (CVZ) advises the government on the delineation of the basic benefit package (College voor Zorgverzekeringen, 2009a).<sup>1</sup> Its mission is to safeguard and develop the public conditions for the health care insurance system so that Dutch citizens can exercise their right to care (College voor Zorgverzekeringen, 2011b). An important task of CVZ is to advise the Dutch Minister of Health on which interventions should be included in the basic benefit package of the Dutch mandatory social health insurance scheme. In an attempt to standardize this procedure, and hence to come to a clear system of package delineation, CVZ has developed a 'package management' framework. The latter consists of four criteria that interventions have to meet if they are to be reimbursed. These criteria are: 1) *necessity*; 2) *effectiveness*; 3) *efficiency* and 4)

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1. Other examples of such institutes are: 1) The National Institute for Clinical Excellence (NICE) in the United Kingdom, 2) Gemeinsamen Bundesausschusses (G-BA) in Germany, 3) Haute Autorité de Santé (HAS) in France, 4) Tandvårds- och läkemedelsförmånsverket (TLF / LFN) in Sweden and 5) Scottish Medicines Consortium (SMC) in Scotland.

*feasibility* (College voor Zorgverzekeringen, 2006). However, in practice, the clarity and degree of operationalization of these criteria differs, which poses challenges to CVZ's aim to apply its criteria consistently.

*Effectiveness* and *efficiency* are operationalized through the measurable and well-known concepts of evidence-based medicine and cost-effectiveness. Although these criteria are not without definitional, operational nor interpretational problems, this is even more so the case for the first and fourth criteria. The fourth criterion (*feasibility*) considers the attainability (from an implementation point of view) and sustainability (from an economic point of view) of including an intervention in the basic benefit package (College voor Zorgverzekeringen, 2006). Hence, the *feasibility* criterion identifies the conditions that need to be met in order for the intervention's inclusion to be attainable and sustainable. The more fundamental desirability of its inclusion, however, is based on the first three criteria.

The operationalization of the first criterion, *necessity*, is also problematic. This criterion entails assessing whether "*the disease or required health care warrants a claim on solidarity given the cultural context*" (College voor Zorgverzekeringen, 2006). The definition and operationalization of the *necessity* criterion has been the topic of much debate and research (e.g. Commissie Criteria Geneesmiddelenkeuze (chair: van Winzum), 1994; Luijn van et al., 1995; Wetenschappelijke Raad voor het Regeringsbeleid, 1997; College voor Zorgverzekeringen, 2001; College voor Zorgverzekeringen, 2006; College voor Zorgverzekeringen, 2009a). It is important to note that the criterion of necessity in the Dutch framework covers two distinct aspects (College voor Zorgverzekeringen, 2009a): (i) 'disease burden' and (ii) 'necessity of insurance' (Nol). Although its exact operationalization remains a matter of discussion, much progress has been made in the quantification of disease burden.<sup>2</sup> This facilitates its use in the process of delineating the basic benefits package. Similar progress has not been witnessed, however, for the Nol-aspect of necessity. Assessing Nol entails the question "*whether it is socially necessary or appropriate to insure an intervention*" (College voor Zorgverzekeringen, 2009a). At present it is relatively unclear what this sub-criterion exactly entails and how it could be used in a systematic way in package management. For instance, while the costs of an intervention at an individual level appears to be an element of Nol (College voor Zorgverzekeringen, 2006) -i.e., it is not necessary to insure against very low cost interventions- much

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2. The operationalization discussion focuses mostly on the issue if disease burden should be measured in an absolute or relative manner. If measured absolutely, the concept of fair innings (Williams, 1997) can be applied. For relative health loss, the concept of proportional shortfall has been proposed (Stolk, Van Donselaar et al., 2004; Van de Wetering, Stolk et al., 2013). CVZ has not formally committed to either one of these concepts yet.

remains unclear when attempting to use this criterion in practice (e.g., the exact level of acceptable costs).

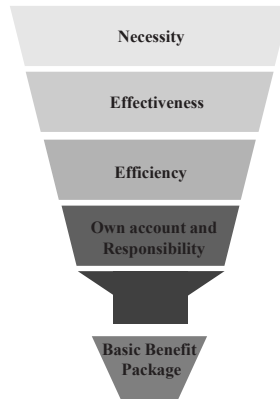
This paper aims to contribute to improving the practical definition and operationalization of the Nol-element of the *necessity* criterion. We report the development of a checklist which can be used in the context of assessing and appraising health care technologies. It enables a structured way of considering the different aspects of the necessity of insurance element, enabling more consistent consideration of these aspects in decision making. The paper is structured as follows. First, we describe the history of the Dutch priority setting process and the Nol-element. Next, we concisely explain CVZ's decision making framework in relation to Nol. Subsequently, we highlight the importance of moving toward a systematic application of Nol drawing on insurance theory, literature and the element's current use in the context of medical aids. From these analyses, we identify the main considerations that should underlie Nol and operationalize them with a checklist, which can be applied in the practice of delineating the basic benefits package.

## 5.2 PRIORITY SETTING AND NOI IN THE NETHERLANDS: A BRIEF HISTORY

The explicitness of the criteria used by CVZ in delineating the basic benefits package is a distinctive feature of the Dutch approach toward priority setting. The Dunning Committee's report from 1991 on choices in health care laid the foundation for this approach and strongly influenced subsequent discussions (Dunning A.J., 1991). The Dunning Committee proposed a clear framework that could be used to decide on which interventions should enter the basic benefit package, based on four criteria. These criteria were 1) *necessity*, 2) *effectiveness*, 3) *efficiency* and 4) *own account and responsibility*. The committee used a powerful image for the use of these criteria in delineating the basic benefits package: the four criteria were depicted as four sieves of a funnel (the so-called 'Funnel of Dunning'). Interventions (consecutively) had to pass all four criteria (sieves) in order to be included in the basic benefits package (Figure 1).

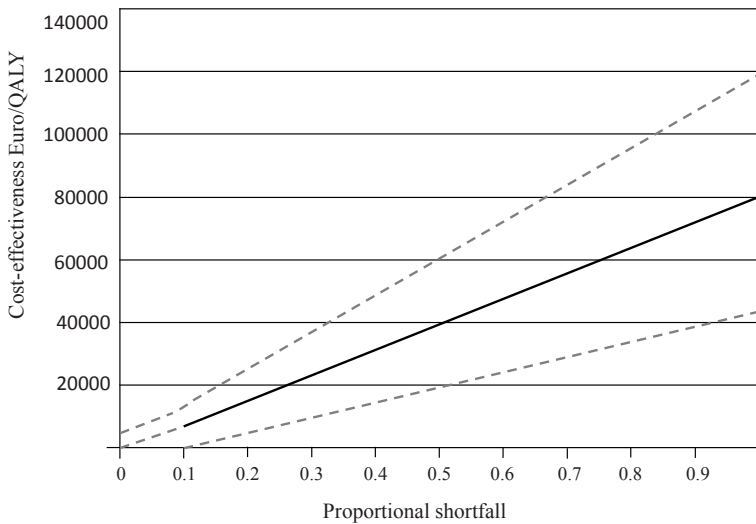
While much progress has been made in operationalizing the criteria put forward by the Dunning committee over the last two decades, it is good to note that the current decision framework is importantly based on Dunning's first three criteria: *necessity*, *effectiveness* and *cost-effectiveness*. This emphasizes the influence the Dunning report has had. The core of the current decision framework can be illustrated as done in Figure 2. In short, it indicates that rather than consecutively, the three main criteria are considered jointly. The idea behind the framework is that the cost-effectiveness threshold -i.e., the amount society is willing to pay per unit of health,





**Figure 1:** The funnel of Dunning

(e.g. per QALY)- increases with disease burden, expressed in some meaningful way, as further highlighted below. Although the exact shape and level of the threshold is unclear, CVZ has indicated a range of 10.000 to 80.000 euros per QALY (6).



**Figure 2:** Proportional Shortfall

While Figure 2 may illustrate the core of the CVZ framework, it is not complete. Dunning's fourth criterion, own account and responsibility (OA&R), is not part of the core. Moreover, it is not a separate criterion anymore in the current CVZ framework. However, the content of the criterion was not dropped. Rather, its underlying considerations became part of the necessity and feasibility criteria. The considerations

relating to the question whether, from an individual/patient perspective, it is necessary and appropriate to insure the intervention, were included in the necessity criterion as the Nol-element. This element is not captured in Figure 2 and less easily quantifiable. Those OA&R considerations which addressed the question whether, from a societal perspective, it is feasible to insure the intervention, were grouped under the *feasibility* criterion, which focuses on macro-affordability and sustainability (College voor Zorgverzekeringen, 2001). Again, these are not part of Figure 2, but may still be important in deciding on whether to include an intervention in the basic benefits package.

### Necessity of Insurance

The Nol-element of the necessity criterion relates to the question, whether, from an individual viewpoint insuring some intervention is necessary and appropriate. Nol captures two important considerations. First of all, the costs of an intervention, i.e., the financial accessibility of the intervention if not insured. The necessity of insuring low-cost, hence affordable care, is less obvious than that of high-cost interventions, *ceteris paribus*. Second, it concerns the appropriateness of health insurance as an instrument to ensure accessibility. For instance, interventions with a high risk of moral hazard<sup>3</sup> may be less easily included in the basic benefits package, as are interventions that are foreseeable. Health insurance is not necessarily the (most) appropriate financing mechanism for such interventions.

Arguably, financial accessibility is the most prominent aspect in determining Nol. Yet, while it may seem a straightforward criterion, using a concept like affordability in practice remains difficult as long as there is no agreement on a reasonable affordability threshold. Furthermore, application of any threshold has been shown to be complicated because what is affordable differs between people, adding to the complexity of operationalizing this concept (Hancock, 1993). Also, settling on a threshold might backfire as suppliers are induced to drive up their prices to just above this threshold as to ensure inclusion (College voor Zorgverzekeringen, 2008a). Nonetheless, in the decision making process in the medical aids sector (as opposed to other sectors like pharmaceuticals), anecdotally, a threshold of €100 is used for consumer products that last. That is, medical aids falling below that threshold were deemed to be affordable and, hence, insurance was deemed inappropriate. For low-cost disposables this threshold is not used. However, it should be noted that low-cost disposables can become unaffordable for patients who need to procure these structurally and often (Niëns & Versteegh, 2011). In what follows we will shortly explain CVZ's current decision making process and the way the Nol-element currently plays a role in it.

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3. The situation whereby patients use more or more expensive care because they are insured.

### 5.3 CVZ'S DECISION MAKING FRAMEWORK AND NOI

CVZ's procedure of advising the government on the in- or exclusion of an intervention currently consists of a two tier process. The intervention's quantitative characteristics are first assessed in an *assessment* phase. In this phase CVZ collects data and consults experts to judge the *effectiveness* and *efficiency* of the intervention, as well as the disease burden (as part of the *necessity* criterion). Together this forms the information required for an assessment as reflected in Figure 3.

For the *NoI*-element and the *feasibility* criterion, justice and solidarity considerations are identified that could influence the reimbursement decision.<sup>4</sup> This is currently not done in a structured way, so that the type of information gathered and the way it is presented can differ between interventions. Together with the information on effectiveness, cost-effectiveness and disease burden, these findings

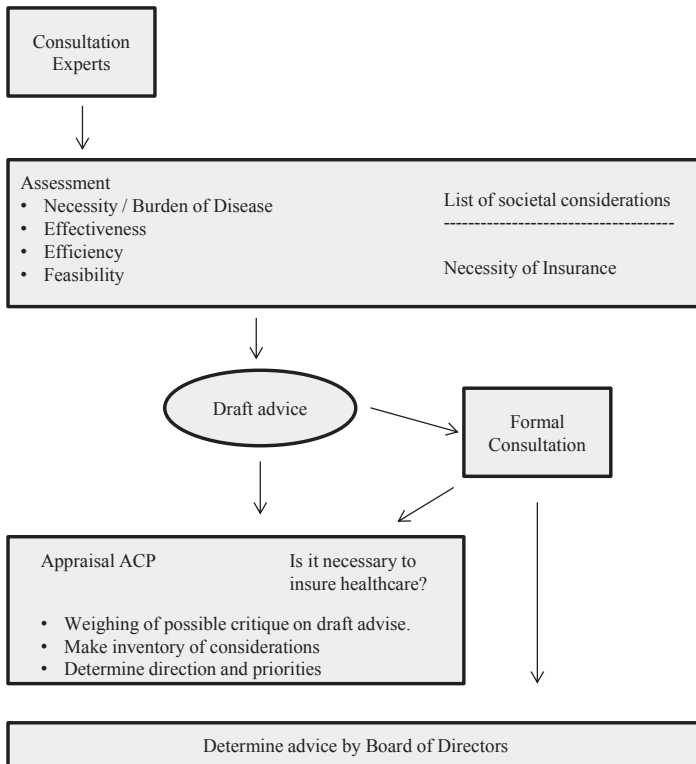


Figure 3: CVZ's package management process

4. In the future CVZ plans to engage the stakeholders in the process of identifying these issues.

are interpreted and presented in a draft advice which is sent to all involved stakeholders for a formal consultation (College voor Zorgverzekeringen, 2006; College voor Zorgverzekeringen, 2009a).

Subsequently, in the *appraisal* phase the draft advice, including stakeholder comments and broader societal considerations, are publicly discussed. This is done in the so-called Package Appraisal Committee (ACP), consisting of a broad range of experts with different professional backgrounds. The ACP evaluates whether the conclusion in the draft advice is not at variance with important broader considerations not captured in the assessment.<sup>5</sup> Besides evaluating this, the ACP also decides which broader considerations are most important, weights the comments of the various stakeholders, and formulates an advice to CVZ's Board of Directors (College voor Zorgverzekeringen, 2009a). Finally, on the basis of the consultation, CVZ's draft advice and the outcome of the ACP-discussion, the Board of Directors decides on the advice to the Minister of Health. This advice will always contain the outcome of the ACP appraisal, even if the final advice is not in line with the ACP appraisal (Figure 3) (College voor Zorgverzekeringen, 2009a).

For the necessity criterion, the subsequent steps are currently followed. In the assessment phase, the disease burden is assessed on the basis of fair innings (Williams, 1997) and proportional shortfall (Stolk et al., 2004; Van de Wetering et al., 2013). Under the fair innings approach, people are considered to be entitled to some 'normal' health achievement. People falling short of this achievement could receive more weight in decision making than people exceeding this achievement. Using proportional shortfall as measure of disease burden, priority can be given to those who, without treatment, stand to lose a larger proportion of remaining health expectancy. Both measures can thus quantify disease burden, using Quality Adjusted Life Years as metric. CVZ currently demands information on both conceptualizations of disease burden, not wishing to adopt one particular measure exclusively. In the appraisal phase, the relevance of both sources of information can be weighed, alongside other potential considerations.

While disease burden therefore is calculated in the assessment phase, this is not the case for necessity of insurance. While this criterion arguably is more pluralistic and less easily quantifiable (College voor Zorgverzekeringen, 2009a), the lack of an instrument to operationalize the Noi-criterion in a structured fashion frustrates its

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5. For Pharmaceuticals the CVZ framework is slightly different. First, all pharmaceuticals are subject to assessment and appraisal by CVZ. Second, for pharmaceuticals a three tier process is applied whereby a commission Pharmaceuticals (CFH) deliberates on the technical assessment before it might be sent to the ACP, which is determined by CVZ. For more info see le Polain et al. (2010).

systematic application and consideration. (The exception to some extent is medical aids, for which the Nol-element is more commonly addressed in the assessment phase (College voor Zorgverzekeringen, 2009a).) Without a structured way of considering necessity of insurance, both in the assessment and the appraisal phase, important aspects may be missed or considered unsystematically. This may negatively influence consistency of decision making. Hence, as a first step in taking the operationalization of the Nol-element forward, we set out to develop a checklist to systematically address the Nol-elements in the assessment phase, thus facilitating a more structured and uniform consideration of these elements in the appraisal phase and decision making. The first step in developing this checklist was to consider the evidence in the literature and practice regarding the relevance, conceptualizations and operationalization of this criterion. This is highlighted in the next section.

#### **5.4 THE IMPORTANCE OF MOVING TOWARD A SYSTEMATIC APPLICATION OF NOI**

In this section we will highlight the rationale for using a Nol-criterion in the delineation of the basic benefits package by drawing on (i) insurance theory; (ii) the published literature regarding (absence of) necessity to insure in the context of health insurance, and (iii) the current use of the criterion in the context of medical aids.

##### **Insurance**

The Nol-criterion relates, first of all, to the rationale of insurance, which is primarily transferring risks over a larger pool (Pauly, 1992; van de Ven, 2009). The mandatory nature of the Dutch social health insurance system ensures solidarity across risk (the healthy subsidize the sick) and income (higher incomes are not compensated for their monthly premiums) (van de Ven & Schut, 2008; van de Ven, 2009). This system guarantees the Dutch population can access necessary treatments the majority could not afford otherwise. This can improve welfare since people derive utility from the financial protection against significant income drops (Nyman, 1999).

However, it is important to critically examine which risks should be insured. Indeed, insurance is not always the most efficient strategy. First, because insurers determine their premiums based on their expected payouts and add to that the loading fee (overhead costs and profit) (Nyman, 1999; van de Ven, 2009). Of course, the lower the cost of the intervention the less sensible it is to accept the loading fee costs as well (de Wit, 1987; College voor Zorgverzekeringen, 2001; van de Ven, 2009). Thus, a rational person will only take out insurance if its benefits outweigh its costs (van de Ven, 2009). Second, if an intervention is almost certainly required by all insured

individuals, insurance is an indirect and potentially inefficient way of paying the intervention. Third, insuring an intervention can lead to moral hazard whereby people use more or more expensive care because it is insured (van de Ven, 2009). When people act as if health care is free of costs, they are bound to consume more than otherwise would have been the case. Although individual premiums do not increase significantly as these additional costs will be spread over all the insured, the impact on total health care costs can be large (de Kam, 2009). It is precisely because the Netherlands has a mandatory health insurance scheme that managing what is being insured is critically important. The insured entitlements should justify the mandatory financial contributions. For example, there are limits to people's willingness to pay for the treatment of conditions with a low disease burden or cost. Thus, in critically assessing the entrance of new interventions in the basic benefits package, CVZ helps to protect Dutch citizens against unnecessary premium increases. As such, CVZ needs to balance equity and efficiency arguments in its advices.

## Literature

Tinghög et al. (2010) present a framework that reverses the necessity of insurance discussion. Instead of looking whether it is necessary to insure an intervention, the authors identify six attributes of medical interventions that jointly preclude the necessity of insurance and therefore may make private financing morally justifiable. Not insuring an intervention in the basic benefit package could be based, according to Tinghög et al. (2010) on the following criteria: 1) there should be sufficient knowledge amongst individuals to value the need and quality of the intervention before and after utilization; 2) there should be sufficient individual autonomy in order to make informed choices regarding the health care they are procuring; 3) there should be low levels of positive externalities from the use of the care; 4) there should be sufficient demand to generate a private market; 5) the interventions should be affordable for most individuals and, finally; 6) the intervention should concern 'lifestyle enhancements' and not 'medical necessities'. In applying their framework, Tinghög et al. (2010) found affordability to be the most important aspect (Tinghög & Carlsson, 2012), which is in line with the experience in the medical aids sector, highlighted next.

## Medical aids

As the Nol-element already plays an important and more systematic role in the review of medical aids, understanding this process might provide pointers for taking forward both its operationalization as well as CVZ's goal of applying its criteria systematically across all interventions. In CVZ's process for reviewing medical aids, the concepts of customary care and financial accessibility play an important role (Col-

lege voor Zorgverzekeringen, 2008a). The concept of customary care is introduced to delineate the boundaries of health insurance, i.e., it emphasizes the fact that only those aids developed especially for people with a disability qualify for reimbursement. Because many medical aids are adapted versions of products that people without disabilities also have to procure, insurance may be considered inappropriate (College voor Zorgverzekeringen, 2009a). An intervention is not deemed customary care (and thus may be added to the benefit package) if it is developed specifically for people with a disability (e.g., medical stockings) and if it is delivered only by certified specialists (e.g., a trained professional is required for fitting hearing aids). If the intervention is deemed 'customary care' the necessity to insure this intervention is lower (College voor Zorgverzekeringen, 2008a). Whether medical aids are financially accessible is assessed by asking three questions. First it is examined whether they substitute for customary products. If so, the need for collective financing decreases (e.g., special cutlery or a bicycle with an add-on motor are substitutes for normal cutlery and a normal bicycle which everybody procures). Second, to ensure their accessibility is guaranteed the medical aid's (additional) costs are assessed. If these are deemed too high for the individual to bear (partial) collective financing is warranted. An example of partial collective financing is expensive orthopedic shoes for which a co-payment of €137.50 (which may be considered reasonable costs for normal shoes) is in place (College voor Zorgverzekeringen, 2012). CVZ recommends higher levels of co-payments if the disability is foreseeable in a normal course of life (e.g., having trouble walking or losing normal visual acuity are 'normal' consequences of growing old). Finally, CVZ evaluates whether the medical aid is related to other already insured interventions which may lead to savings or quality issues (e.g., although a stocking aid for putting on medical stockings is cheap, it increases the compliance of wearing them which will offset other costs in the future). In reviewing the reimbursement of medical aids, CVZ assesses all aspects of customary care and financial accessibility jointly. Hence, no single aspect is a priori decisive.

All aspects highlighted above were taken into account in developing the checklist for Nol.

## 5.5 CHECKLIST

In an effort to increase the transparency, consistency, and comprehensiveness of the appraisal discussion regarding the Nol-element, together with the assessors of interventions at CVZ, we developed a checklist that structures the main considerations identified in the previous paragraphs. We did so taking a patient perspective, which is in line with CVZ's procedure of taking into account the costs of the intervention at

the individual level (College voor Zorgverzekeringen, 2006) under the Nol-element of the necessity criterion. This is in line with the guidelines for reviewing medical aids, in which the patient perspective is also leading (College voor Zorgverzekeringen, 2009a). For matters of consistency we tried to stay close to the nomenclature used in assessing the reimbursement of medical aids where, as discussed, the 'necessity of insurance' considerations already play a more systematic role. The checklist was not intended to lead to clear-cut decision regarding in- or exclusion of the intervention under study. Rather, its contribution should lie in providing transparency and structure in the application of the Nol-element in CVZ's package management, e.g. facilitating structured debates in the ACP and leading to consistent consideration of these issues in decision making.

Drawing from insurance theory, literature and CVZ's experience in the medical aids sector, as a first step in this process we developed a preliminary checklist that was sent to the assessors of interventions at CVZ for discussion. An iterative process ensued in which, based on their input regarding the scope and content of the considerations underlying Nol, as well as their interpretation of the questions posed, we further developed the instrument. This process led to a checklist consisting of two themes with four questions each (Figure 4). The questions in the 'health insurance as an instrument theme' all address issues that are specifically related to the rationale for and consequences of health insurance. Hence, the issues of 'moral hazard', the fact that some ailments can be foreseen (thereby reducing the logic of insurance), and paternalistic motives in case positive or negative public health spill-over effects are to be expected (e.g. better public health due to tests for sexually transmitted diseases being provided free of cost) are addressed here. The theme of 'financial accessibility' looks at the costs of an intervention from an individual perspective and

<p><b>Health insurance as an instrument</b></p> <ul style="list-style-type: none"> <li>• Is the intervention customary care?</li> <li>• Is the intervention foreseeable?</li> <li>• Might there be under-usage of an intervention if it is not insured?</li> <li>• Might be over-usage of an intervention if it is insured (moral hazard)?</li> </ul> <p><b>Financial accessibility</b></p> <ul style="list-style-type: none"> <li>• Does the intervention substitute for something that the large majority of the population also uses?</li> <li>• Can the (additional) treatment costs be borne by the individual patient?</li> <li>• Can the patient expect relevant savings (offsetting the costs) due to the intervention?</li> <li>• Are treatment costs incurred only once or are structural in character?</li> </ul>
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Figure 4: CVZ/IMTA checklist



asks if the patient can be expected to bear these costs. Historically, in the Netherlands, it has been difficult to agree on an absolute financial threshold below which interventions do not enter the benefit package (Luijn van et al., 1995). Moreover, setting one threshold fitting all circumstances seems unlikely to be realized. Hence, three questions address additional and contextual reasons why collective financing might not be required. These concern: (i) substitution, whereby an intervention substitutes for something the general population also uses/buys; (ii) whether the patient potentially saves money due to the intervention, which would (partially) offset the costs of the intervention and (iii) whether the costs are incurred only once or more often.

### Putting it to the test

To see whether this checklist can be used in practice to structure the information regarding, and debate on the NoI-element (in the ACP), it was tested retrospectively on 10 different health care interventions. In Table 1, for each of the 10 interventions, the eight questions are answered. Finally, before we show the current reimbursement policy, we also list the decision that would be based on the NoI-element of the necessity criterion only.

Table 1 shows that the first four interventions, all medical aids -i.e., reading glasses, rollator walker, watch for the visually impaired, lift chair-, are currently not reimbursed. While CVZ deemed reading glasses (#1) and the rollator walker (#2) to be customary care -i.e., they do not meet the requirements of both being specifically for people with an ailment/disability and delivery by trained specialists only-, watches for the visually impaired (#3) and smoking cessation programs (#4) were not deemed customary care. Furthermore, the (additional) costs of these four medical aids were deemed bearable for the individual patient. Whereas for reading glasses this was the main argument for exclusion, for the rollator walker, the watch for the visually impaired and the lift chair the substitution argument played an important role as well. The lift chair by far is the most expensive of these interventions. However, CVZ argued that furniture in general is expensive and because it is foreseeable that people at some point in time will have more difficulties standing up they can anticipate this when buying new furniture (College voor Zorgverzekeringen, 2008b). The fifth intervention, smoking cessation programs (#5), is presently reimbursed. These programs were removed from the package in 2012 (Stivoro, 2013) with relevant savings for patients -i.e., they would not have to spend their money on tobacco anymore- being the main political argument for doing so. In this case, CVZ's advice to reimburse these programs (based on favorable cost-effectiveness (Parrott et al., 1998; Feenstra et al., 2005; Hoogendoorn et al., 2010) and smoking's large burden of disease (College voor Zorgverzekeringen, 2009b)) was neglected. Since

Table 1: checklist applied to 10 different health care interventions

Question / intervention	1	2	3	4	5	6	7	8	9	10
	Reading glasses	Rollator walker	Watch for visually impaired	Lift chairs	Smoking cessation programs	Codeine	Infiximab	Incontinence materials	Orthopedic shoes	Floppy ear correction
1 Customary Care?	yes	yes	no	no	no	no	no	no	no	no
2 Is the intervention foreseeable?	only farsightedness	yes	no	yes	maybe	no	no	no	no	no
3 under-usage if not insured?	maybe	no	maybe	maybe	depends on	maybe	no	no	maybe	no
4 over-usage if insured?	maybe	yes	no	yes	yes - insurance might have people enroll more often	no	no	maybe	no	yes
5 Substitution?	no	yes - bike	yes - normal watch	yes - normal chair	no	no	no	no	yes - regular shoes	no
6 Can (additional) costs be borne by individual patient?	yes	yes	yes	yes	maybe	yes	no	maybe	no	yes
7 Are relevant savings to be expected for patient?	no	no	no	no	yes - no cigarettes are bought	no	no	no	no	no
8 Costs incurred once or structural?	once every few years	once	once	once	once	once	structural	structural	once every few years	once
Reimbursement decision based on NoI only	NOT reimbursed	NOT reimbursed	NOT reimbursed	NOT reimbursed	NOT reimbursed	Reimbursed	Reimbursed	not clear	not clear	NOT reimbursed
Current reimbursement decision	NOT reimbursed	NOT reimbursed	NOT reimbursed	NOT reimbursed	Reimbursed	Reimbursed	Reimbursed	co-payment of €75 per year	co-payment of €137.50 if >16 / €69.50 if < 16 years of age	NOT reimbursed

2013 however, these interventions have entered the benefit package again because their usage had dropped significantly (Stivoro, 2013). Interventions six and seven -i.e. Codeine (#6) and Infliximab (#7)- should be reimbursed when judged solely on the basis of the Nol-element, which is in line with the current reimbursement policy. Applying the Necessity criterion, CVZ deemed incontinence materials (#8) for pure stress-incontinence not to meet the requirements for reimbursement, i.e., the disease burden was too low. As other types of incontinence would not be characterized by a low disease burden and distinguishing between these groups is not possible, CVZ recommended a co-payment for all incontinence materials of €75 per year. As this approximately equals the yearly amount that people with mild incontinence issues pay, CVZ stated that the financial accessibility of incontinence materials did not decrease (College voor Zorgverzekeringen, 2011a). Because orthopedic shoes (#9) substitute for regular shoes, CVZ recommended installing a fixed co-payment as the additional costs of this footwear are too high for people to bear (College voor Zorgverzekeringen, 2012). Finally, a floppy ear correction (#10) is seen as a cosmetic intervention the costs of which can be borne by the individual patient.

These examples show that it is possible to systematically address the identified considerations underlying the Nol-element and the checklist could inform appraisal discussions in a structured way.

## 5.6 DISCUSSION

The Dutch Healthcare Insurance Board has developed a framework of four criteria to guide decisions on reimbursement of healthcare interventions. Applying this framework consistently in practice turned out to be challenging, however. Although much progress has been witnessed over the last years in operationalizing specific criteria, this has been less the case for the sub-criterion of necessity to insure. Both in terms of the criterion's conceptual clarity as in terms of its measurability, much remained unclear. This paper aimed to address the latter issues by highlighting the elements included in the criterion necessity to insure, as well as its place in the decision making framework. Moreover, we presented a newly developed checklist for Nol that allows it to be applied both systematically and package-broad.

Grouped in the two themes of health insurance as an instrument and financial accessibility, the proposed checklist introduces eight questions which address the most relevant issues to see whether it is necessary to insure an intervention from the individual level. Its anticipated users are decision makers at CVZ who prepare assessment reports which serve as input for the ACP. Through that process, the checklist facilitates systematic discussion of the Nol-element of the necessity criterion in the

ACP. This ensures the process of these discussions to be transparent and understandable while its outcomes are replicable, thereby limiting arbitrariness to a minimum. Currently, the checklist is being implemented in CVZ's package management framework where it will be used in assessing interventions.

Of course the framework has some limitations as well. Most notably, it does not answer the question how much people can and/or should pay themselves. Implementing a financial threshold below which interventions should not be reimbursed is a political decision. Through ability to pay studies (Russell, 1996; Van Doorslaer et al., 2006) scholars could provide politicians and policy makers with information on the range within which such a threshold should fall. Secondly, although the checklist provides transparency, consistency and comprehensiveness in the process of addressing CVZ's Nol-element, the operationalization of its questions is broad and does not provide concrete help in answering these questions. Therefore, incremental but continuous improvement of the checklist is required. A third limitation is the fact that, more often than not, filling out the checklist does not provide a clear cut answer regarding reimbursement decisions. It merely signals a possible problem that needs to be discussed in the appraisal phase. The weighing of the various considerations would be an important question for future research.

The implications of the checklist will mostly concern the process of decision making. Increasing transparency, consistency and comprehensiveness will give more legitimacy to the decisions made by policy makers (Daniels & Sabin, 1997; Daniels, 1999). When the retrospective analysis of actual decisions being taken is an indication, Nol's impact on future reimbursement decisions will be limited, i.e., most decisions in Table 1 are in line with the expected outcome if Nol alone was decisive in decision making. Rather, the decisions can be explained better and are more predictable.

Governments face increasingly difficult decisions on entitlements because they are accountable for both ensuring that people's mandatory financial contributions are employed justifiably as well as guaranteeing the financial accessibility of their health care systems. For the Nol-element of the *necessity* principle, the proposed checklist is a first step in providing transparency, consistency and comprehensiveness in these decisions.



# PART III

Health Economics at the Macro Level  
in Low- and Middle-income Countries:  
Choices in Breast Cancer and HIV/AIDS





# Chapter 6

## Cost-Effectiveness of Breast Cancer Control Strategies in Central America: The Cases of Costa Rica and Mexico

*Submitted Article*





## ABSTRACT

This paper reports the most cost-effective policy options to support and improve breast cancer control in Costa Rica and Mexico.

Total costs and effects of breast cancer interventions were estimated using the health care perspective and WHO-CHOICE methodology. Effects were measured in disability-adjusted life years (DALYs) averted. Costs were assessed in 2009 United States Dollars (US\$). To the extent available, analyses were based on locally obtained data from the Caja Costaricensse de Seguro Social (CCSS – national health insurance system) and the Ministry of Health (MoH) in Costa Rica and the Unidad de Analisis Económico (UAE) of the MoH in Mexico.

In Costa Rica, the current strategy of treating breast cancer in stages I to IV at a 80% coverage level seems to be the most cost-effective with an incremental cost-effectiveness ratio (ICER) of US\$4,739 per DALY averted. At a coverage level of 95%, biennial clinical breast examination (CBE) screening could improve Costa Rica's population health twofold, and can still be considered very cost-effective (ICER US\$5,964/DALY). For Mexico, our results indicate that at 95% coverage a mass-media awareness raising program (MAR) could be the most cost-effective (ICER US\$5,042/DALY). If more resources are available in Mexico, biennial mammography screening for women 50-70yrs (ICER US\$12,718/DALY), adding Trastuzumab (ICER US\$13,994/DALY) or screening women 40-70yrs biennially plus Trastuzumab (ICER US\$17,115/DALY) are less cost-effective options.

We recommend both Costa Rica and Mexico to engage in MAR, CBE or mammography screening programs, depending on their budget. The results of this study should be interpreted with caution however, as the evidence on the intervention effectiveness is uncertain. Also, these programs require several organizational, budgetary and human resources, and the accessibility of breast cancer diagnostic, referral, treatment and palliative care facilities should be improved simultaneously. A gradual implementation of early detection programs should give the respective Ministries of Health the time to negotiate the required budget, train the required human resources and understand possible socioeconomic barriers.

## 6.1 INTRODUCTION

Due to population ageing and changing lifestyles in low-and-middle countries (LMICs), breast cancer incidence rates are increasing (Althuis et al., 2005; Parkin & Fernandez, 2006). Given the organizational and financial constraints faced by the health systems in LMICs the majority of breast cancers are diagnosed at late stages (Agarwal et al., 2009). Accordingly, the majority of breast cancer deaths occur in LMICs (Porter, 2008; Ferlay et al., 2010). The World Health Organization (WHO) therefore states that early detection and implementation of cost-effective interventions should be a priority in LMICs (World Health Organization, 2012a). In an attempt to support LMICs with breast cancer control, the Susan G. Komen for the Cure foundation provided a grant to investigate the cost-effectiveness of several breast cancer control interventions in seven LMICs<sup>1</sup> to a consortium of the WHO, Erasmus University Rotterdam (EUR) and Radboud University Nijmegen Medical Center (RUNMC). Cost-effectiveness analyses may support governments in deciding how to spend scarce resources in health care most efficiently.

In each country, during four phases, the consortium works closely with local authorities and experts in the fields of breast cancer, health economics, epidemiology and public policy. First, a three-day technical workshop is held, where the consortium explains a general cost-effectiveness model based on WHO-CHOICE methodology (described elsewhere (Tan-Torres Edejer et al., 2003; Groot et al., 2006)) which is to be tailored to the country specific situation. In the second phase, lasting approximately six months, local authorities identify and assemble the (local) data required for the cost-effectiveness model. Subsequent in phase three, the cost-effectiveness analyses are carried out. Thereafter, a second workshop is organized. Here the results of the analyses are discussed among representatives of all local institutions involved in breast cancer care and made available for actual policy making by the local health authorities, i.e., the fourth phase. This paper identifies the most cost-effective interventions for breast cancer control in both Costa Rica and Mexico from a health care perspective.

After presenting an overview of the situation regarding breast cancer in both Costa Rica and Mexico, we discuss the methods, data and interventions considered in this study and discuss the results.

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1. Costa-Rica, Mexico, Brazil, Colombia, Ghana, India, Peru.

## 6.2 BREAST CANCER IN COSTA RICA AND MEXICO

Cancer incidence and mortality rates are rising across Central America (Robles & Galanis, 2002; González-Robledo et al., 2010). In Costa Rica and Mexico breast cancer ranks among the top-five causes of death for women over 25 years old (Knaul et al., 2008). Between 1995 and 2003, breast cancer incidence increased by 32.3% to a rate of 40.07 per 100,000 women in Costa Rica (Ministerio de Salud, 2007). In Mexico, breast cancer incidence increased as well and in both countries breast cancer mortality rates have increased since the 1980s (López-Ríos et al., 1997; Robles & Galanis, 2002; Martínez-Montañez et al., 2009). In Costa Rica 13.14 breast cancer deaths per 100,000 women in 2006 were observed, the highest number among malignant neoplasms. Mortality rates per 100,000 women range from 28.19 in the province Dota to 1.23 in Guácimo, while in the provinces Los Chiles, La Cruz, and Garabito no breast cancer related deaths were registered (Ministerio de Salud, 2007). In Mexico mortality rates doubled over the last 20 years. The average mortality rate per 100,000 women in Mexico stands at 9.9 with regional differences ranging from 13.2 and 11.8 in the Federal District and the north, respectively, to 9.7 and 7.0 in the center and the south of the country, respectively (Palacio-Mejía et al., 2009). This increase caused breast cancer to overtake cervical cancer as the most deadly cancer among females in 2006 (Martínez-Montañez et al., 2009; Palacio-Mejía et al., 2009). Where in 1979 1,144 females died from the disease, in 2006 4,497 deaths were registered (Palacio-Mejía et al., 2009).

Although in Costa Rica and Mexico official recommendations for both breast self-examination (BSE) and mammography screening have existed for over a decade, their coverage levels remain very low and the large majority of breast cancer patients present at the hospital with advanced disease (Ministerio de Salud, 2000; Franco-Marina et al., 2009; Knaul et al., 2009).

In light of the above, Non-Governmental Organizations (NGOs) and the general public put pressure on governments in Costa Rica and Mexico to improve treatment and early diagnosis through screening (Fundacion Nacional de Solidaridad Contra el Cancer de Mama, 2011; Fundación Cim\*ab, 2011). Hence, both countries face choices on efficient allocation of scarce resources for breast cancer screening.

## 6.3 METHODS AND DATA

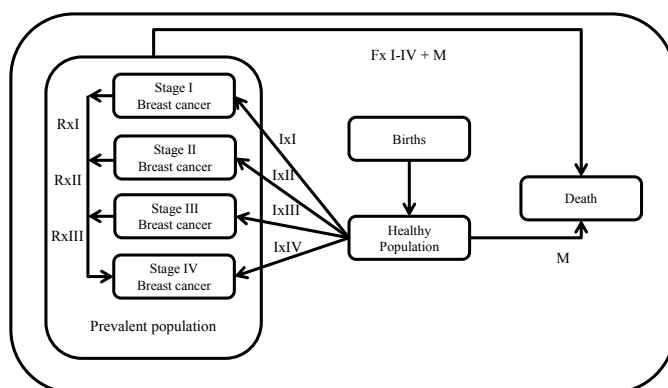
### General approach

We used the WHO-CHOICE methodology, described in detail elsewhere (Tan-Torres Edejer et al., 2003; Groot et al., 2006), as a basis of our analysis. This approach com-

compares all possible interventions in a specific disease area to a situation where no interventions are implemented. The latter, a counterfactual 'null scenario', acts as a reference to compare the costs and effects of existing and new interventions. An intervention in isolation, or a combination of different interventions, is then implemented for 10 years in a modeled population. However, to include effects that occur after these 10 years, this modeled-population is tracked for 100 years. This approach enabled us to make comparisons of the costs and health effects across a wide range of competing interventions, identify differences in relative cost-effectiveness and identify the most efficient mix of interventions to improve population health.

### Breast Cancer Model

Costs and health effects are calculated using a state transition population model developed and explained in detail by Groot et al. (2006). Its structure is presented in Figure 1 (Groot et al., 2006). The model simulates the development of a national population and accounts for births, background mortality and breast cancer epidemiology of a country. It includes a healthy state, a deceased state, and stage I to IV breast cancer states following the classification of the American Joint Committee on Cancer (AJCC) (Greene et al., 2006). The effectiveness of each intervention is expressed in changes in disability weights (DWs, i.e., health state valuations (HSVs)), case fatality rates (CFs, i.e., improved survival for treatment scenarios), or in more positive stage distributions (in awareness raising and screening interventions). Since the interventions affect mortality (CFs) and morbidity (DWs), intervention effectiveness is expressed in disability adjusted life years (DALYs) averted. The difference in



**Figure 1:** Graphical representation of the model showing the relationships between the different health states through the incidence rates of breast cancer ( $Ix1$ – $Ix4$ ), the different stage specific case fatality rates ( $Fx1$ – $Ix4$ ), and the background mortality ( $M$ ) (Groot et al., 2006). Stage specific relapse rates to stage IV were used to correct health state valuations only ( $Rx1$ – $Rx3$ )

the total number of healthy years lived by the population between each scenario and the null-scenario gives the population health gains in DALYs averted.

Zelle et al. (2012) improved the published model (Groot et al., 2006) by correcting HSVs for relapse, assuming that patients could only relapse to stage IV at a constant rate (Adjuvant Online, 2010). This rate was calculated as the average over the 10 year period in which the interventions were implemented. Although the probability of relapse normally decreases over time, Zelle et al. (2012) calculated the average rate because the model does not allow for different relapse rates over time. As a result, while the relapse rates are underestimated in early and overestimated in later years, the average amount of relapsed patients after 10 years is approximately the same.

### **Interventions**

An important element of the overall project is to select a set of appropriate interventions for breast cancer control in LMICs. Therefore, a study group at WHO-CHOICE defined a mix of 11 common and preferable practices in 2009 (Zelle et al., 2012). Participating countries can combine and adapt these practices to appropriately inform their specific policy questions. For Costa Rica and Mexico focus was placed on the cost-effectiveness of screening and treatment combinations. The most urgent policy questions in both countries concerned the age groups that should be targeted for screening and whether treating Her2/NEU+ patients with Trastuzumab (Herceptin™) was cost-effective. Therefore, the basic awareness raising intervention was excluded and different intervention scenarios, including treatment with Trastuzumab, were added. Combining the 11 common practices with or without Trastuzumab led to a total of 19 scenarios. The current situations of breast cancer control in Costa Rica and Mexico were modeled at 80% and 70% geographic coverage levels -i.e., reaching 80% and 70% of those people who need services- respectively. All other interventions were evaluated at a geographic coverage level of 95%. An overview of the interventions is listed in Table 1.

### **Effectiveness**

A key factor is the stage distribution of patients presenting at the hospital, given that the breast cancer stage determines the survival and disability of a patient and the effectiveness of each intervention (Greene et al., 2006).

In Costa Rica we obtained the current stage distribution from Ortiz (Ortiz, 2007), who studied breast cancer survival in Costa Rica between 2000 and 2003. Demographic data and incidence rates were obtained from the Statistical office of the Costa Rican MoH. For the prevalence we used the 2004 Global Burden of Disease estimates (World Health Organization, 2008b).

**Table 1:** Definition and classification of individual interventions (coverage) (based on (Zelle et al., 2012)).

Treatment of individual stages	Down-staging interventions <sup>b</sup>	Palliative care <sup>d</sup>
Stage I treatment: lumpectomy with axillary dissection and radiotherapy. Eligible patients receive tamoxifen <sup>a</sup> or chemotherapy <sup>e</sup> (Anderson et al., 2006; Groot et al., 2006; Adjuvant Online, 2010).	Basic Awareness Raising (BAR): community nurses training program + opportunistic outreach activities by community nurses to raise breast cancer awareness and educate on breast self-examination techniques (BSE) + enhanced media activities (Devi, 2007). <sup>c</sup>	Basic Palliative Care (BPC): palliative care volunteers training program + home-based visits by volunteers every fortnight + pain treatment through morphine, laxatives and palliative radiotherapy (8 Gy in 1 fraction) for eligible patients (Anderson et al., 2006; Devi, 2007; Kumar, 2007).
Stage II treatment: lumpectomy with axillary dissection and radiotherapy. Eligible patients receive tamoxifen <sup>a</sup> or chemotherapy <sup>e</sup> (Anderson et al., 2006; Groot et al., 2006; Adjuvant Online, 2010).	Mass-media awareness raising (MAR): BAR + mass media campaign (Devi, 2007).	Extended Palliative Care (EPC): BPC apart from community nurses instead of palliative care volunteers, pain treatment strengthened with antidepressants, anti-emetics and zelodronic acid (Hortobagyi, 2002; Anderson, 2006; Walsh & Ribycki, 2006; Devi, 2007; Kumar, 2007).
Stage III treatment: modified mastectomy followed by adjuvant chemotherapy <sup>e</sup> and radiotherapy <sup>f</sup> . Eligible patients receive tamoxifen <sup>a</sup> (Anderson et al., 2006; Groot et al., 2006).	Biennial clinical breast examination (CBE) screening in asymptotically women aged 40–69 years: community nurses training program + active outreach screening by community nurses + limited media activities (Zotov et al., 2003; Devi, 2007).	
Stage IV treatment: adjuvant Chemotherapy <sup>e</sup> and radiotherapy (10 Gy) + end of life hospitalization. Eligible patients receive total mastectomy and/or tamoxifen <sup>a</sup> (Khan et al., 2002; Anderson et al., 2006).	Biennial mammography screening in asymptomatic women aged 50–69 years + limited media activities (Groot et al., 2006).	
Treatment of stage I – IV as listed above plus the addition of Trastuzumab <sup>g</sup> for Her2/NEU+ patients.	Biennial mammography screening in asymptomatic women aged 40–69 years + limited media activities (Groot et al., 2006). <sup>c</sup>	

<sup>a</sup> Endocrine therapy consists of 20 mg tamoxifen per day for 5 years.

<sup>b</sup> Down-staging interventions cause a shift in stage distribution and are only modeled in combination with treatment of all stages (I–IV).

<sup>c</sup> BAR was excluded as a standalone intervention in Costa Rica and Mexico

<sup>d</sup> Palliative care interventions are only applied to stage IV patients, and substitutes stage IV treatment.

<sup>e</sup> The (neo)adjuvant chemotherapy combination regimen consists of 7 cycles of Epirubicin, Fluorouracil and cyclophosphamide (FEC regimen) Given on an outpatient basis.

<sup>f</sup> Radiotherapy includes a standard dose of 50 Gy given in 25 fractions of 2 Gy on an outpatient basis.

<sup>g</sup> Trastuzumab is given for 8 months.

Table 2: Analyzed interventions and the effectiveness estimates used

Costa Rica (CR) - Intervention	Case Fatality Rates <sup>a</sup>				Disability Weights <sup>b</sup>				Stage Distribution <sup>c</sup>			
	stage I	Stage II	Stage III	Stage IV	stage I	Stage II	Stage III	Stage IV	stage I	% in stage II	% in stage III	% in stage IV
Untreated	0.0207	0.0654	0.1556	0.3112	0.086	0.097	0.104	0.375	14.6%	41.6%	20.4%	23.4%
Stage I treatment	0.0056				0.086				14.6%			
Stage II treatment		0.0393				0.097				41.6%		
Stage III treatment			0.0930				0.104				20.4%	
Stage IV treatment				0.2750				0.154				23.4%
Basic Palliative Care (BPC)				0.2750				0.153				23.4%
Extended Palliative Care (EPC)				0.2750				0.152				23.4%
Current Country Situation	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	14.6%	41.6%	20.4%	23.4%
Mass-media Awareness Raising (MAR)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	21.1%	41.5%	24.1%	13.3%
Biennial CBE screening (40-69)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	32.0%	34.3%	25.8%	7.9%
Biennial mammography screening (50-69)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	35.0%	37.5%	21.1%	6.5%
Biennial mammography screening (40-69)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	40.0%	42.8%	13.2%	4.0%
With Trastuzumab	0.0050	0.0353	0.0835	0.2470	0.086	0.097	0.104	0.154				

Table 2: Analyzed interventions and the effectiveness estimates used (continued)

Mexico(MX) - Intervention	Case Fatality Rates <sup>a</sup>				Disability Weights <sup>b</sup>				Stage Distribution <sup>c</sup>			
	stage I	Stage II	Stage III	Stage IV	stage I	Stage II	Stage III	Stage IV	% in stage I	% in stage II	% in stage III	% in stage IV
Untreated	0.0207	0.0654	0.1556	0.3112	0.086	0.097	0.104	0.375	13.8%	39.6%	33.9%	12.7%
Stage I treatment	0.0056				0.086				13.8%			
Stage II treatment		0.0393				0.097				39.6%		
Stage III treatment			0.0930				0.104				33.9%	
Stage IV treatment				0.2750				0.154				12.7%
Basic Palliative Care (BPC)				0.2750				0.153				12.7%
Extended Palliative Care (EPC)				0.2750				0.152				12.7%
Current Country Situation	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	13.8%	39.6%	33.9%	12.7%
Mass-media Awareness Raising (MAR)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	21.1%	41.5%	24.1%	13.3%
Biennial CBE screening (40-69)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	30.5%	32.6%	28.3%	8.7%
Biennial mammography screening (50-69)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	33.9%	36.3%	22.8%	7.0%
Biennial mammography screening (40-69)	0.0056	0.0393	0.0930	0.2750	0.086	0.097	0.104	0.154	39.1%	41.8%	14.6%	4.5%
With Trastuzumab	0.0054	0.0374	0.0865	0.2569	0.086	0.097	0.104	0.154				

<sup>a</sup> Estimates for stages III and IV from Groot et al. (2006); for stages I and II from Zelle et al. (2012). CFs for untreated patients are from Groot et al. (2006) and were corrected based on Bloom et al. (1962). <sup>b</sup> Estimates from Zelle et al. (2012). <sup>c</sup> Current situation CR: based on Ortiz (2007); MX: Knaul et al. (2009); Effects MAR derived from Devi (2007); Effects screening interventions were based on stage shifts from baseline Groot et al. (2006) to the stage distribution USA in Bland et al. (1998). Stage shifts were adapted by calculating relative differences in detection rates between the USA and CR / MX from Duffy & Gabe (2005). Calculations included age-specific incidence (MoH CR & UAE MX), prevalence (WHO 2008), sojourn time (Duffy & Gabe, 2005), sensitivity (Bobo, Lee et al., 2000) and attendance (75% in the USA vs. 80% in Costa Rica and Mexico).



For Mexico, we used the current stage distribution from Knaul et al. (2009), who studied 1904 patients that were all treated within the Mexican Social Security Institute (IMSS, its abbreviation in Spanish). Demographic data were obtained from the Mexican National Population Council (Consejo Nacional de Población, 2011). For Mexico we obtained incidence rates based on GLOBOCAN 2008 adjusted by age-group considering the distribution from the Mexican Histopathology Registry 2006 (Secretaría de Salud de Mexico - Dirección General de Epidemiología, 2006; International Agency for Research on Cancer, 2012). For the prevalence in Mexico, as in Costa Rica, we used 2004 Global Burden of Disease estimates (World Health Organization, 2008b).

The case fatality rates for the treatment scenarios were based on Groot et al. (2006) (stage III & IV) and Zelle et al. (2012) (stage I & II), who corrected those from Groot et al. (2006) for the use of chemotherapy in stage I and II. We take these CF's to represent technical efficiency, representing the maximum amount of DALYs that can be averted based on successful implementation of breast cancer diagnosis, treatment and follow-up strategies.

Since screening and awareness interventions as defined in international literature, alter the stage distribution, their effects on the stage distribution at presentation were estimated using the same methods applied by Zelle et al. (2012). Zelle et al. (2012) used international study results to estimate the health effects of various screening options and accounted for the sensitivity of the screening method, attendance rates (80% in both countries), incidence rates and demography in target groups.

## Costs

In line with the WHO-CHOICE approach we distinguished patient, program and training costs, which were calculated by multiplying quantities of applied procedures by their corresponding unit costs. Patient costs were dependent on patient consumption (utilization) of explicit resources (procedures) for diagnosis, treatment, follow-up, early detection and screening.

Although Costa Rica has developed several guidelines for treating breast cancer over the years (Ministerio de Salud, 2000; Ministerio de Salud, 2009), local specialists informed us that treatments differ somewhat across hospitals. Therefore, together with these specialists, we revised the entire set of resource items to reflect the (average) current breast cancer treatment practices in Costa Rica. Specialists in Mexico had a similar opinion. As its health care system has three main public institutions

providing health care,<sup>2</sup> treatment and reimbursement between these institutions may differ due to, for example, differences in salaries and drug prices. Hence we used resource utilization estimates of IMSS, which provides social insurance to approximately 40% of Mexico's population (Knaul & Frenk, 2005).

Whenever possible we used locally obtained costing data. When not available we applied the original WHO-CHOICE estimates for either country. These estimates are based on econometric analysis of a detailed WHO-CHOICE database from South Africa including a set of standard salaries, drugs, outpatient visits, materials and supplies, capacity utilization and transportation multipliers (WHO Department of Essential Health Technologies, 2005). In Costa Rica, the CCSS provided readily available unit costs of most breast cancer procedures. For Mexico, contrary to Salomon et al. (2012), who used the WHO-CHOICE original estimates on costs, in this study we used a detailed micro-costing exercise performed by IMSS (Instituto Mexicano del Seguro Social, Unidad Análisis Económico, 2012).

Costs of the procedures used for Costa Rica and Mexico are listed in Table 3. We also integrated evaluation costs of women presenting without breast cancer, included the costs of diagnosing all other stages (for stages I-IV separately) and, regarding screening interventions, included costs for evaluating false positives.

For the program-level costs, which capture management, administrative, media and law-enforcement costs, as well as costs for training of healthcare personnel, we used local salaries and WHO-CHOICE allocation rules for Costa Rica. For Mexico we used the standard WHO-CHOICE program cost estimates and allocation rules. Media and operating costs -i.e., prices for broadcasting, flyers, and posters- were provided by the CCSS in Costa Rica and the MoH in Mexico.

Training costs were primarily based on training the required health care workers for each intervention. We maintained the allocation assumptions listed in the WHO-CHOICE model as set by Zelle et al. (2012) and used local salaries and WHO standard salaries for Costa Rica and Mexico respectively. In both countries all costs were estimated in 2009 local currency units —i.e., Costa Rican colones (CRC) and Mexican pesos (MXN)- and converted to U.S. dollars (US\$) using the 2009 exchange rate (1.00US\$ = 560.45CRC and 1.00US\$ = 13.06MXN\$) (Oanda, 2013; The World Bank Group, 2013c). Both health effects (DALYs) and costs (US\$) were discounted at

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2. - Instituto Mexicano del Seguro Social (IMSS) – covers salaried workers in the private sector.
  - Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado (ISSSTE) – provides benefits for government workers.
  - Seguro Popular – voluntary public insurance for non-salaried workers or the unemployed.

**Table 3:** Average utilization of diagnosis and treatment ingredients and unit costs per patient.

Procedure	Ingredients	Stage I		Stage II		Stage III		Stage IV		Relapse		Palliative Care <sup>g</sup> (Extended)		Unit cost per patient (US\$)	
		Costa Rica	Mexico	Costa Rica	Mexico	Costa Rica	Mexico	Costa Rica	Mexico	Costa Rica	Mexico	Costa Rica	Mexico	Costa Rica	Mexico
Initial diagnosis and evaluation during treatment	No. of health center visits	1	1	1	1	1	1	1	1	1	1	1	1	23,69 <sup>a</sup>	25,40 <sup>c</sup>
	No. of hospital visits	3	2	3	2	3	2	3	2	3	2	3	2	63,187 <sup>a</sup>	80,47 <sup>c</sup>
	Bilateral Mammography	1	1	1	1	2	1	-	-	-	-	-	-	45,44 <sup>a</sup>	42,27 <sup>d</sup>
	Complete blood count	7	7	7	7	7	7	7	7	6	6	6	6	17,50 <sup>b</sup>	10,34 <sup>d</sup>
	FNA or core needle biopsy	1	1	1	1	1	1	1	1	-	-	-	-	71,62 <sup>a</sup>	91,52 <sup>c</sup>
	Liver function tests	8	8	8	8	8	8	8	8	7	7	7	7	40,31 <sup>a</sup>	10,34 <sup>d</sup>
	Ultrasonography	1	1	1	1	1	1	1	1	-	-	-	-	23,65 <sup>b</sup>	48,32 <sup>d</sup>
	Renal function tests	8	8	8	8	8	8	8	8	7	7	7	7	9,81 <sup>a</sup>	10,34 <sup>d</sup>
	Bone scan	-	-	-	-	1	1	1	1	1	-	-	-	108,01 <sup>b</sup>	192,57 <sup>d</sup>
	Chest X-ray	1	1	1	1	1	1	1	1	1	-	-	-	16,11 <sup>a</sup>	14,93 <sup>c</sup>
Non-breast cancer evaluation	ECG	1	1	1	1	1	1	1	1	1	1	1	1	10,14 <sup>b</sup>	27,26 <sup>f</sup>
	Her2/neu test	1	1	1	1	1	1	1	1	1	1	1	1	27,73 <sup>e</sup>	32,70 <sup>d</sup>
	No. of health center visits	2	2	2	2	2	2	2	2	2	2	2	2	23,69 <sup>a</sup>	25,40 <sup>c</sup>
	Bilateral Mammography	1	1	1	1	1	1	1	1	1	1	1	1	45,44 <sup>a</sup>	42,27 <sup>d</sup>
	Ultrasonography	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	0.28	22,68 <sup>b</sup>	22,59 <sup>c</sup>
	FNA or core needle biopsy	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	71,62 <sup>b</sup>	91,52 <sup>c</sup>
	No. of hospitalization days	2	2	2	2	2	2	2	2	6	0	6	0	134,55 <sup>a</sup>	292,11 <sup>c</sup>
	No. of OPD visits radiotherapy	30	0	30	0	30	0	30	0	30	0	30	0	63,16 <sup>a</sup>	80,47 <sup>c</sup>

Table 3: Average utilization of diagnosis and treatment ingredients and unit costs per patient. (continued)

Procedure	Stage I	Stage II	Stage III	Stage IV	Relapse	Palliative Care <sup>g</sup> (Extended)	Unit cost per patient (US\$)
No. of OPD visits	6	7	6	7	6	7	63,16 <sup>a</sup> 80,47 <sup>c</sup>
chemotherapy	Lumpectomy	Lumpectomy	Lumpectomy	Lumpectomy	Lumpectomy	Lumpectomy	239,33 <sup>b</sup> 805,59 <sup>c</sup>
% receiving surgical intervention	60%	80%	40%	20%	-	-	-
	Mastectomy	Mastectomy	Mastectomy	Mastectomy	Mastectomy	Mastectomy	243,27 <sup>b</sup> 857,34 <sup>d</sup>
	40%	20%	40%	60%	10%	10%	5%
% receiving anesthesia	100%	100%	100%	100%	10%	-	-
% receiving radiotherapy	70%	86%	70%	80%	100%	30%	61,22 <sup>b</sup> 76,68 <sup>c</sup>
	61%	50%	61%	61%	61%	40%	50%
% receiving endocrine treatment <sup>i</sup>	-	80%	20%	100%	60%	80%	1469,97 <sup>a</sup> 2327,20 <sup>c</sup>
% receiving boost radiotherapy <sup>k</sup>	-	80%	20%	100%	60%	80%	71,23 <sup>b</sup> 106,16 <sup>c</sup>
% receiving home based visits	-	80%	20%	100%	60%	80%	23,69 <sup>a</sup> 25,40 <sup>c</sup>
% receiving morphine <sup>l</sup>	-	80%	20%	100%	60%	80%	0,59/day <sup>a</sup> 1,12 <sup>c</sup>
% receiving laxative <sup>m</sup>	-	80%	20%	100%	60%	80%	0,10/day <sup>a</sup> 0,03 <sup>c</sup>
% receiving Ondansetron <sup>n</sup>	-	80%	20%	100%	60%	80%	2,80/day <sup>a</sup> 1,72 <sup>c</sup>
% receiving Amitriptyline <sup>o</sup>	-	80%	20%	100%	60%	80%	0,04 <sup>a</sup> 0,37 <sup>c</sup>
% receiving Zolodronic Acid <sup>p</sup>	-	80%	20%	100%	60%	80%	200,00 <sup>a</sup> 260,18 <sup>d</sup>
% receiving Trastuzumab	30%	11%	30%	14%	30%	30%	1800 <sup>a</sup> 1610 <sup>c</sup>

<sup>a</sup> Based on estimates by Costa Rican CCSS. <sup>b</sup> Unit costs WHO-CHOICE database in 2000 US\$. Corrected for inflation: 2000-2009 (2.81 in CR & 1.66 in MX). 2009 exchange rates were used (560.45 CRC/US\$ & 13.06 MXN/US\$) - Based on values of IMSS. <sup>c</sup> Based on communication with UAE of MoH. <sup>d</sup> Based on Norum et al. (2005). <sup>e</sup> Based on Knaul et al. (2008). <sup>f</sup> palliative care (substitutes stage IV treatment). <sup>g</sup> 50 Gy given in 25 fractions of 2 Gy. <sup>h</sup> daily dose of 20 mg. Tamoxifen for 5 years. <sup>i</sup> 7 cycles of Epirubicin, Fluorouracil and cyclophosphamide (FEC regimen). <sup>k</sup> 1 fraction of 10 Gy. <sup>l</sup> 40ml/54days. <sup>m</sup> 35mg/54 days. <sup>n</sup> 8mg/day. <sup>o</sup> 75mg/day. <sup>p</sup> 5 mg/day

a rate of 3% annually, which is recommended by WHO-CHOICE (Tan-Torres Edejer et al., 2003).

### **Cost-effectiveness analysis**

The average cost-effectiveness ratio (ACER) of each intervention is calculated by dividing the average costs of the intervention by the average number of DALYs averted. These ACERs provide information on the set of interventions a region should finance to maximize health gains. The incremental cost-effectiveness ratios (ICERs) are calculated in relation to the last intervention purchased in each country, by dividing the incremental costs by the incremental health effects. These ICERs are used to establish an expansion path which shows the order in which the various interventions should be introduced if cost-effectiveness is the only consideration (Evans et al., 2005). Only interventions with the lowest cost for additional effects are considered on this expansion path. WHO-CHOICE defines interventions that have a cost-effectiveness ratio of less than one times the gross domestic product (GDP) per capita as very cost-effective, and those with a ratio that falls between one and three times the GDP per capita as cost-effective (World Health Organization, 2012b). In Costa Rica, this means that interventions that cost less than US\$6,629 per DALY averted can be considered very cost-effective, and interventions that cost between US\$6,629 and US\$19,888 per DALY averted can be considered cost-effective. For Mexico these thresholds are US\$8,416 and US\$25,249 per DALY averted, respectively.

### **Sensitivity analysis**

In line with Zelle et al. (2012) we performed a deterministic sensitivity analysis for both Costa Rica and Mexico to assess the impact of key parameters on our cost-effectiveness estimates. In both countries we increased the DW's with 10%. Whereas costs of outpatient visits were increased by 25%, we raised the costs of mammography with 200%. In estimating the impact of various screening interventions we decreased the sensitivity of CBE and mammography by 25% and assumed screening attendance rates of 60%. When available we also used alternative stage distributions for the current situation and different CFs. The unit costs for surgical procedures in Costa Rica were much lower than those of Mexico. To test the impact of this we substituted these costs with the Mexican values.

## 6.4 RESULTS

Table 4 shows the results for Costa Rica (panel A) and Mexico (panel B). Both costs, effects and cost-effectiveness are presented. In Figure 2 these results are presented graphically, the expansion paths are shown as black lines.

### Costa Rica

Table 4 panel A shows the annual number of DALYs averted in treating the individual stages I-IV to vary between 193 (stage III) and 573 (stage II). Jointly these interventions in each stage can avert almost 1,400 DALYs per year. Adding palliative care only averts a small number of DALYs. The costs of treating the individual stages range between approximately US\$4 million and US\$5 million per year. Adding basic and extensive palliative care programs to stage IV treatment adds approximately US\$0.1 and US\$1 million to the yearly costs of stage IV treatment. At the 80% coverage level the current country situation in Costa Rica is highly cost-effective with an ICER below the country's GDP per capita, i.e., US\$4,739/DALY. In expanding Costa Rica's breast cancer services, our analysis shows that treatment of all stages plus a CBE screening program targeting women between 40 and 70 years of age (I-IV + CBE (40-70)) is the next best option. At a total yearly cost of almost US\$13 million, CBE averts 2,381 DALYs per year. This can be considered a very cost-effective intervention as the ICER of this intervention is below Costa Rica's GDP per DALY.

From figure 2 it follows that although the ACER of implementing mammography screening for women between 50-70 years is still below Costa Rica's GDP per capita per DALY, the ICER (as compared to CBE screening) is not lower than this threshold, i.e., the slope of the expansion path is steeper than US\$6,629/DALY. While still considered a cost-effective intervention, mammography screening in age group 50-69 averts 2,619 DALYs per year at a yearly cost of US\$16 million. Increasing the age group for mammography screening to women between 40-70 years shows a similar trend, i.e., averting 3,015 DALYs at an annual cost of US\$21 million can be considered cost-effective. Adding Trastuzumab to this intervention, while resulting in the highest number of DALYs averted per year -i.e., 3,274 DALYs at a total yearly cost of US\$29 million-, is not considered cost-effective as its ICER is higher than three times the GDP per DALY.

The combinations of various interventions are all close to the expansion path meaning they avert DALYs at a slightly less favorable ICER but could nevertheless be meaningful to implement. For example, expanding the current program's coverage to reach 95% or implementing a Mass-media Awareness Raising program (MAR), could be interesting options if the available budget is not sufficient to implement a screening strategy.

Table 4: Average costs (US\$), effects and cost-effectiveness of breast cancer control scenarios per year

Panel A: Costa Rica										
No.	Description of intervention	Patients per year	Annual patient costs <sup>a</sup>	Annual program costs	Annual training costs	Annual total costs	DALYs averted per year <sup>b</sup>	ACER <sup>c</sup>	ICER <sup>d</sup>	
1	Current country specific situation (80%)	940	4,569,310	646,358	6,660	5,222,329	1,102	4,739	4,739	
2	Stage I to IV treatment (current) + Trastuzumab (80%)	940	11,708,670	646,358	6,660	12,361,689	1,347	9,180	NA	
3	Stage I treatment + relapse (95%)	163	2,862,111	854,431	7,439	3,723,980	404	9,218	NA	
4	Stage II treatment + relapse (95%)	464	4,303,195	854,431	7,439	5,165,065	573	9,007	NA	
5	Stage III treatment + relapse (95%)	227	3,884,520	854,431	7,439	4,746,390	193	24,587	NA	
6	Stage IV treatment (95%)	261	3,107,345	854,431	7,439	3,969,215	162	24,559	NA	
7	Basic Palliative Care (BPC) (95%)	261	2,466,328	1,583,922	27,897	4,078,147	163	25,078	NA	
8	Extended Palliative Care (EPC) (95%)	261	3,160,703	2,022,956	27,897	5,211,556	164	31,852	NA	
9	Stage I to IV treatment combined (current 95%)	1,116	5,659,297	1,421,412	7,439	7,088,148	1,309	5,417	NA	
10	Biennial mammography screening (50-70) + treatment of stage I to IV (95%)	1,116	12,498,059	3,792,653	22,317	16,313,029	2,619	6,228	NA	
11	Biennial mammography screening (50-70) + treatment of stage I to IV + Trastuzumab (95%)	1,116	20,438,042	3,792,653	22,317	24,253,012	2,886	8,402	NA	
12	Biennial mammography screening (40-70) + treatment of stage I to IV (95%)	1,116	17,546,792	3,792,522	22,317	21,361,632	3,015	7,085	13,426	
13	Biennial mammography screening (40-70) + treatment of stage I to IV + Trastuzumab (95%)	1,116	25,401,093	3,792,522	22,317	29,215,932	3,274	8,924	30,352	
14	Basic awareness outreach program + Mass-media Awareness Raising (MAR) + treatment of stage I to IV (95%)	1,116	6,158,209	4,519,154	11,159	10,688,521	1,825	5,857	NA	
15	Biennial Clinical Breast Examination (CBE) screening (40-70) + treatment of stage I to IV (95%)	1,116	9,255,065	3,576,629	20,086	12,851,779	2,381	5,397	5,964	
16	MAR + BPC + treatment of stage I to III (95%)	1,116	6,262,398	4,733,109	39,055	11,034,563	1,826	6,044	NA	

**Table 4:** Average costs (US\$), effects and cost-effectiveness of breast cancer control scenarios per year (continued)

Panel A: Costa Rica										
No.	Description of intervention	Patients per year	Annual patient costs <sup>a</sup>	Annual program costs	Annual training costs	Annual total costs	DALYs averted per year <sup>b</sup>	ACER <sup>c</sup>	ICER <sup>d</sup>	
17	Biennial CBE Screening + BPC + treatment of stage I to III (95%)	1,116	9,422,391	3,426,610	47,982	12,896,984	2,382	5,415	NA	
18	Biennial mammography Screening (40-70) + BPC + treatment stage I to III (95%)	1,116	17,578,700	4,170,935	50,214	21,799,850	3,016	7,229	NA	
19	Biennial mammography Screening (50-70) + EPC + treatment of stage I to III (95%)	1,116	12,620,626	4,215,537	50,214	16,886,376	2,621	6,444	NA	

<sup>a</sup> All costs in this Table are in 2009 US\$ (1CRC = 0,001784 US\$).

<sup>b</sup> DALYs, disability-adjusted life-years (age weighted, discounted).

<sup>c</sup> ACER: Average cost-effectiveness ratio compared to the do nothing-scenario (US\$ per DALY averted).

<sup>d</sup> ICER: Incremental cost effectiveness ratio, ratio of additional cost per additional life-year saved when next intervention is added to a mix on the intervention path (additional US\$ per additional DALY saved).



**Table 4:** Average costs (US\$), effects and cost-effectiveness of breast cancer control scenarios per year (continued)  
**Panel B:** Mexico

No.	Description of intervention (coverage level)	Patients per year	Annual patient costs <sup>a</sup>	Annual program costs	Annual training costs	Annual total costs	DALYs averted per year <sup>b</sup>	ACER <sup>c</sup>	ICER <sup>d</sup>
1	Current country specific situation (70%)	12,682	105,806,655	2,015,857	18,055	107,840,567	18,870	5,715	NA
2	Stage I to IV treatment (current) + Trastuzumab (70%)	12,682	156,929,320	2,015,857	18,055	158,963,231	21,645	7,344	NA
3	Stage I treatment + relapse (95%)	2,375	65,738,476	2,514,872	18,958	68,272,306	7,993	8,541	NA
4	Stage II treatment + relapse (95%)	6,815	103,978,996	2,514,872	18,958	106,512,826	10,629	10,021	NA
5	Stage III treatment + relapse (95%)	5,834	87,447,510	2,514,872	18,958	89,981,341	6,015	14,960	NA
6	Stage IV treatment (95%)	2,186	71,452,527	2,514,872	18,958	73,986,358	1,503	49,231	NA
7	Basic Palliative Care (BPC) (95%)	2,186	53,723,979	15,215,345	71,094	69,010,419	1,513	45,609	NA
8	Extended Palliative Care (EPC) (95%)	2,186	101,903,885	16,563,415	71,094	118,538,394	1,523	77,813	NA
9	Stage I to IV treatment combined (current 95%)	17,211	144,702,484	3,698,580	18,958	148,420,023	25,609	5,796	NA
10	Biennial mammography screening (50-70) + treatment of stage I to IV (95%)	17,211	277,083,624	33,291,106	56,875	310,431,605	44,192	7,025	12,718
11	Biennial mammography screening (50-70) + treatment of stage I to IV + Trastuzumab (95%)	17,211	324,996,119	33,291,106	56,875	358,344,101	47,616	7,526	13,994
12	Biennial mammography screening (40-70) + treatment of stage I to IV (95%)	17,211	389,559,667	33,287,097	56,875	422,903,640	50,714	8,339	NA
13	Biennial mammography screening (40-70) + treatment of stage I to IV + Trastuzumab (95%)	17,211	434,231,086	33,287,097	56,875	467,575,059	53,998	8,659	17,115
14	Basic awareness outreach program + Mass-media Awareness Raising (MAR) + treatment of stage I to IV (95%)	17,211	149,329,898	15,890,849	28,438	165,249,184	32,777	5,042	5,042
15	Biennial Clinical Breast Examination (CBE) screening (40-70) + treatment of stage I to IV (95%)	17,211	227,545,334	32,896,957	51,188	260,493,479	39,769	6,550	NA
16	MAR + BPC + treatment of stage I to III (95%)	17,211	186,985,021	29,692,145	99,532	216,776,698	32,787	6,612	NA

**Table 4:** Average costs (US\$), effects and cost-effectiveness of breast cancer control scenarios per year (continued)  
**Panel B:** Mexico

No.	Description of intervention (coverage level)	Patients per year	Annual patient costs <sup>a</sup>	Annual program costs	Annual training costs	Annual total costs	DALYs averted per year <sup>b</sup>	ACER <sup>c</sup>	ICER <sup>d</sup>
17	Biennial CBE Screening + BPC + treatment of stage I to III (95%)	17,211	247,889,383	31,257,913	122,282	279,269,578	39,778	7,021	NA
18	Biennial mammography Screening (40-70) + BPC + treatment stage I to III (95%)	17,211	400,120,033	41,081,697	127,970	441,329,699	50,722	8,701	NA
19	Biennial mammography Screening (50-70) + EPC + treatment of stage I to III (95%)	17,211	296,212,416	41,169,323	127,970	337,509,708	44,210	7,634	NA

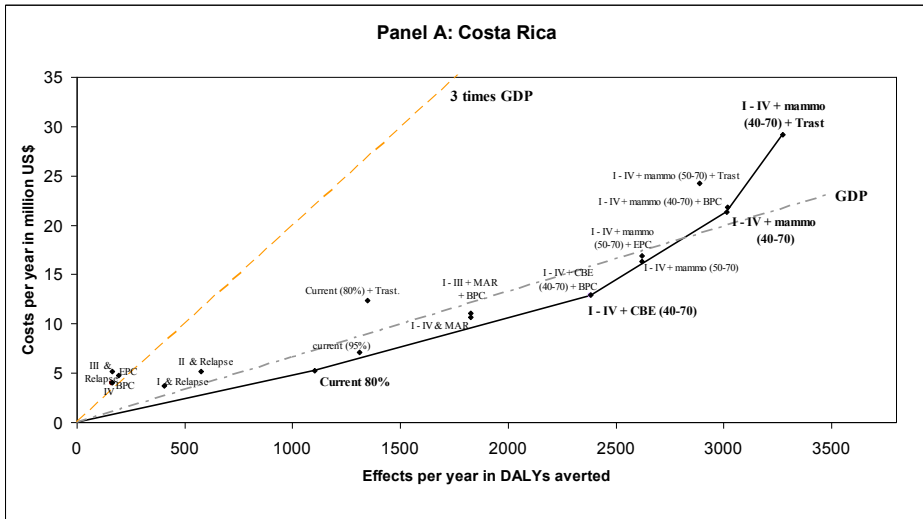
<sup>a</sup> All costs in this Table are in 2009 US\$ (1MXN = 0,0765697 US\$).

<sup>b</sup> DALYs, disability-adjusted life-years (age weighted, discounted).

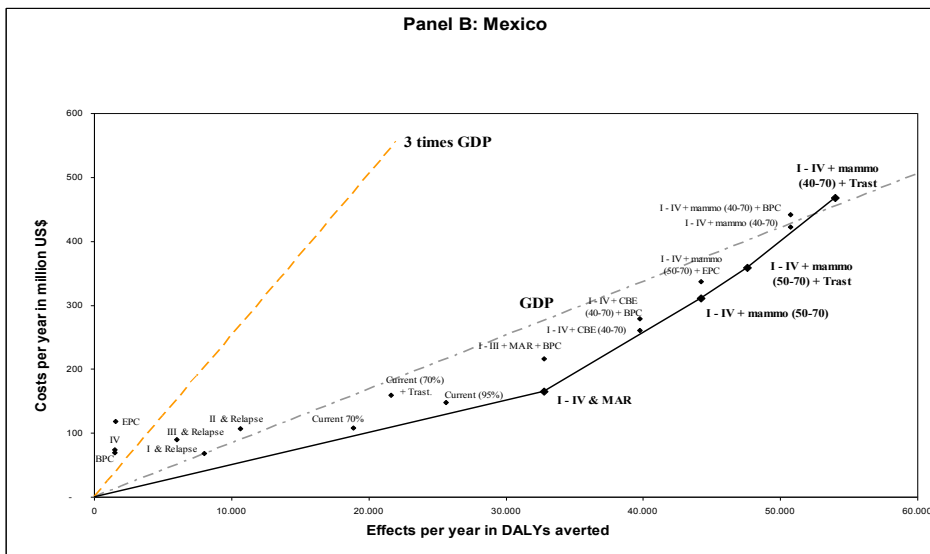
<sup>c</sup> ACER: Average cost-effectiveness ratio compared to the do nothing-scenario (US\$ per DALY averted).

<sup>d</sup> ICER: Incremental cost effectiveness ratio, ratio of additional cost per additional life-year saved when next intervention is added to a mix on the intervention path (additional US\$ per additional DALY saved).

**Figure 2: Cost-effectiveness of breast cancer interventions and expansion path according to Incremental Cost-Effectiveness Ratios (ICERs) for Costa Rica & Mexico**



Dotted lines represent cost-effectiveness threshold of 1 and 3 times 2009 GDP/capita, i.e., 6,629 US\$/DALY and 19,888 US\$/DALY (Oanda, 2013; The World Bank Group, 2013c).



Dotted lines represent cost-effectiveness threshold of 1 and 3 times 2009 GDP/capita, i.e., 8,416 US\$/DALY and 25,249 US\$/DALY (Oanda, 2013; The World Bank Group, 2013c).

## Mexico

Table 4 panel B shows that the annual number of DALYs averted in the individual stages I-IV varies between 1,503 (stage IV) and 10,629 (stage II). Jointly these interventions in each stage avert approximately 26,000 DALYs per year. The addition of palliative care does not gain much health.

With an ACER of US\$5,715 the current situation with 70% coverage is very cost-effective. The analysis shows it is better to increase the coverage level of the current intervention to 95% rather than add Trastuzumab. In our analysis, implementing a program of Mass-media awareness raising (MAR) buys health most efficiently. Our results show that MAR averts 32,777 DALYs per year at a yearly cost of US\$165 million, which leads to an ACER of US\$5,042 per DALY averted.<sup>3</sup> If a higher budget were available, implementing mammography screening for women aged 50-70 would be the first next step. This intervention averts 44,192 DALYs per year at an estimated yearly cost of US\$310 million. Even more resources would allow subsequently adding Trastuzumab and increasing the age group to 40-70. These interventions fill out the expansion path and avert 47,616 and 50,714 DALYs per year at an estimated yearly cost of US\$358 and US\$471 million respectively. It should be noted that a CBE screening program, with an expected health gain of 39,769 DALYs averted at a cost of US\$260 million, could be an interesting 'in-between' option.

## Sensitivity analysis

Sensitivity analysis showed our results to be particularly sensitive to different assumptions on stage distribution at presentation and case fatality rates (Table 5). The Costa Rican CFs we obtained from Ortiz (Ortiz, 2007) differed strongly from those we deem to reflect technical efficiency (Groot et al., 2006; Zelle et al., 2012). Using these CFs causes the ACERs to vary between minus 82.7% for stage I and plus 65.5% for stage II. With regards to the current stage distribution, for Costa Rica we used the distribution from Groot et al. (2006). With this less favorable stage distribution, the current country situation was no longer part of the expansion path. Rather, the CBE screening program now became the most cost-effective.

For Mexico we ran the model with three different current stage distributions obtained from different studies (Groot et al., 2006; Flores-Luna et al., 2008; Comisión

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3. It should be noted that we estimate the MAR intervention to lead to a fixed stage distribution (see also: Zelle et al. (2012)). Although by implementing MAR in Mexico, the proportion of patients in stage IV actually goes up, we decided to include this intervention nonetheless because the total number of DALYs averted are substantially higher than the effects of the current country situation. This is due to the strong improvement in the proportions of patients in stage I and decrease in stage III (the proportion in stage II improves slightly).

**Table 5:** Results of sensitivity analysis on average cost-effectiveness ratio (ACER)  
**Panel A:** Costa Rica

<b>Intervention scenarios</b>	<b>ACER</b>	<b>Alternative stage distribution<sup>a</sup></b>	<b>Case fatality rates<sup>b</sup></b>	<b>Disability weights +10%</b>	<b>Costs outpatient visits +25%</b>	<b>Costs mammo-graphy +200%</b>	<b>Costs mastec-tomy Mexico</b>	<b>Costs lumpec-tomy Mexico</b>	<b>Capacity utilization equipment -25%<sup>c</sup></b>	<b>Sensitivity of CBE and mammography -25%<sup>d</sup></b>	<b>Attendance screening program 60%</b>
<b>1</b> Current country specific situation 80%	4,739	5,519	4,447	5,132	4,882	6,218	4,931	4,901	4,739		
<b>2</b> Stage I to IV treatment combined (current 80%) + Trastuzumab	9,180	9,838	8,226	9,796	9,325	10,402	9,337	9,313	9,180		
<b>3</b> Stage I treatment	9,218	11,569	53,348	13,846	9,690	13,096	9,308	9,340	9,218		
<b>4</b> Stage II treatment	9,007	16,395	5,442	9,605	9,369	12,032	9,183	9,250	9,007		
<b>5</b> Stage III treatment	24,587	7,630	19,686	26,352	25,608	33,092	25,133	24,709	24,587		
<b>6</b> Stage IV treatment	24,559	29,195	25,869	26,307	25,774	33,715	24,646	24,559	24,559		
<b>7</b> Basic Palliative Care (BPC)	25,078	30,875	26,412	26,833	26,248	34,179	25,121	25,078	25,078		
<b>8</b> Extended Palliative Care (EPC)	31,852	38,068	33,542	34,044	33,245	40,897	31,895	31,852	31,852		
<b>9</b> Stage I to IV treatment combined (current 95%)	5,417	6,254	5,082	5,866	5,592	6,895	5,609	5,579	5,417		
<b>10</b> Biennial mammography screening (50-70 years) + Stage I to IV treatment	6,228	4,464	7,060	6,565	6,538	10,589	6,336	6,330	6,228	7,535	7,723
<b>11</b> Biennial mammography screening (50-70 years) + Stage I to IV treatment + Trastuzumab	8,402	6,251	9,013	8,807	8,684	12,365	8,501	8,495	8,402	9,856	10,058
<b>12</b> Biennial mammography screening (40-70 years) + Stage I to IV treatment	7,085	5,216	8,069	7,433	7,496	13,203	7,174	7,182	7,085	7,677	8,114
<b>13</b> Biennial mammography screening (40-70 years) + Stage I to IV treatment + Trastuzumab	8,924	6,769	9,674	9,322	9,303	14,562	9,006	9,014	8,924	9,566	10,031

Table 5: Results of sensitivity analysis on average cost-effectiveness ratio (ACER) (continued)

Panel A: Costa Rica

Intervention scenarios	ACER	Alternative stage distribution <sup>a</sup>	Case fatality rates <sup>b</sup>	Disability weights +10%	Costs outpatient visits +25%	Costs mammo-graphy +200%	Costs mastec-tomy Mexico	Costs lumpec-tomy Mexico	Capacity utilization equipment -25% <sup>c</sup>	Sensitivity of CBE and mammography -25% <sup>d</sup>	Attendance screening program 60%
14 Mass media awareness raising (MAR) + treatment of stage I to IV	5,857	3,965	5,947	6,247	6,017	7,232	6,010	5,987	5,857		
15 Biennial clinical breast examination (CBE) screening (40–69) + treatment of stage I to IV	5,397	3,794	6,095	5,710	5,916	5,977	5,520	5,503	5,397	6,881	7,028
16 MAR + BPC + Stage I to III treatment	6,044	4,092	6,137	6,446	6,206	7,418	6,195	6,174	6,044		
17 Biennial CBE screening (40–69) + BPC + treatment of stage I to III	5,415	3,806	6,115	5,728	5,934	5,994	5,537	5,520	5,415	6,919	7,068
18 Biennial mammography screening (40–69) + BPC + treatment of stage I to III	7,229	5,323	8,232	7,583	7,641	13,345	7,318	7,326	7,229	7,836	8,284
19 Biennial mammography screening (50–69) + EPC + treatment of stage I to III	6,444	4,619	7,304	6,792	6,756	10,803	6,551	6,545	6,444	7,815	8,013

<sup>a</sup> Alternative stage distribution: 9.4% stage I, 14.2% stage II, 58.0% stage III, 18.4% stage IV (Groot, Baltussen et al., 2006). <sup>b</sup> Alternative CFs; 0,0174 stage I, 0,0284 stage II, 0,0832 stage III, 0,2855 stage IV (Ortiz, 2007). <sup>c</sup> Mechanical equipment (e.g. mammography machines, CT, X-ray). <sup>d</sup> Lower effectiveness of awareness interventions (-25%), sensitivity of CBE, + stage shifts CBE screening.

## Panel B: Mexico

Intervention scenarios		ACER	Alternative stage distribution <sup>a</sup>	Alternative stage distribution <sup>b</sup>	Alternative stage distribution <sup>c</sup>	Case fatality rates <sup>d</sup>	Disability weights +10%	Costs outpatient visits +25%	Costs mammo-graphy +200%	Capacity utilization equipment -25% <sup>e</sup>	Sensitivity of CBE and mammography -25% <sup>f</sup>	Attendance screening program 60%
1	Current country specific situation 70%	5,715	6,081	6,576	5,742	7,696	7,764	5,865	6,861	5,713		
2	Stage I to IV treatment combined (current 70%) + Trastuzumab	7,344	7,405	7,330	7,513	9,031	8,768	7,482	8,400	7,342		
3	Stage I treatment	8,541	11,835	11,407	9,745	19,263	11,997	8,933	11,407	8,534		
4	Stage II treatment	10,021	9,613	9,026	16,334	11,433	14,721	10,326	12,416	10,014		
5	Stage III treatment	14,960	12,661	15,139	9,786	18,509	31,038	15,515	19,071	14,950		
6	Stage IV treatment	49,231	55,817	169,157	37,773	46,698	52,548	51,336	63,668	49,192		
7	Basic Palliative Care (BPC)	45,609	53,896	195,026	31,995	43,268	48,621	47,661	59,946	45,569		
8	Extended Palliative Care (EPC)	77,813	85,844	229,906	62,358	73,858	82,886	80,085	92,056	77,774		
9	Stage I to IV treatment combined (current 95%)	5,796	6,168	6,673	5,820	7,804	7,874	5,946	6,942	5,793		
10	Biennial mammography screening (50-70 years) + Stage I to IV treatment	7,025	5,703	8,161	4,043	9,059	7,649	7,397	11,541	7,023	10,041	10,567
11	Biennial mammography screening (50-70 years) + Stage I to IV treatment + Trastuzumab	7,526	6,261	8,495	4,607	9,462	8,108	7,526	7,526	7,526	10,051	10,460
12	Biennial mammography screening (40-70 years) + Stage I to IV treatment	8,339	6,992	9,425	5,169	10,572	8,945	8,863	15,109	8,338	9,525	10,509
13	Biennial mammography screening (40-70 years) + Stage I to IV treatment + Trastuzumab	8,659	7,377	9,599	5,602	10,859	9,226	9,148	14,974	8,658	9,821	10,688

## Panel B: Mexico

Intervention scenarios	ACER	Alternative stage distribution <sup>a</sup>	Alternative stage distribution <sup>b</sup>	Alternative stage distribution <sup>c</sup>	Case fatality rates <sup>d</sup>	Disability weights +10%	Costs outpatient visits +25%	Costs mammo-graphy +200%	Capacity utilization equipment -25% <sup>e</sup>	Sensitivity of CBE and mammography -25% <sup>f</sup>	Attendance screening program 60%
14 Mass media awareness raising (MAR) + treatment of stage I to IV	5,042	3,671	6,530	2,303	6,604	5,822	5,193	6,211	5,040		
15 Biennial clinical breast examination (CBE) screening (40–69) + treatment of stage I to IV	6,550	5,149	7,837	3,510	8,579	7,246	7,218	7,097	6,549	11,097	11,711
16 MAR + BPC + Stage I to III treatment	6,612	4,816	8,568	3,021	8,661	7,634	6,763	7,718	6,610		
17 Biennial CBE screening (40–69) + BPC + treatment of stage I to III	7,021	5,519	8,402	3,763	9,195	7,766	7,690	7,568	7,019	12,194	12,893
18 Biennial mammography screening (40–69) + BPC + treatment of stage I to III	8,701	7,296	9,836	5,394	11,023	9,333	9,226	15,490	8,700	10,010	11,103
19 Biennial mammography screening (50–69) + EPC + treatment of stage I to III	7,634	6,200	8,874	4,395	9,844	8,312	8,009	12,149	7,633	11,152	11,765

<sup>a</sup> UAE - 8.4% stage I, 38.5% stage II, 42.5% stage III, 10.6% stage IV (Comisión Nacional de Protección Social en Salud, 2011). <sup>b</sup> 9.7% stage I, 52.7% stage II, 34.8% stage III, 2.8% stage IV (Flores-Luna et al., 2008). <sup>c</sup> 9.4% stage I, 14.2% stage II, 58.0% stage III, 18.4% stage IV (Groot et al., 2006). <sup>d</sup> Alternative Case Fatality rates: 0.013 stage I, 0.042 stage II, 0.102 stage III, 0.266 stage IV (Salomon et al., 2012). <sup>e</sup> Mechanical equipment (e.g. mammography machines, CT, X-ray). <sup>f</sup> Lower effectiveness of awareness interventions (-25%), sensitivity of CBE, + stage shifts CBE screening.



Nacional de Protección Social en Salud, 2011). These different stage distributions caused the ACERs to increase between 0 – 15%. When using the higher CFs from Salomon et al. (2012) for the intervention scenarios, the ACERs increased to a greater extent (34.7% for the current country situation).

For both countries, changes in the other parameters also led to different outcomes although the impact was smaller. For example, in Costa Rica the WHO default unit costs for a mastectomy or a lumpectomy were relatively low. Unable to obtain these unit costs from Costa Rica, using the higher Mexican unit costs showed their impact on the ACERs to be marginal.

## 6.5 DISCUSSION

Our results indicate that in both Costa Rica and Mexico treating stage IV disease only, or treating stage IV and providing basic or extended palliative care is not cost-effective. In general, interventions ensuring more patients to present at the hospital in earlier stages seem the most cost-effective.

These results are in line with other studies which find mammography screening for women aged 50-70 to be cost-effective in sub-Saharan Africa and South East Asia (Groot et al., 2006; Ginsberg et al., 2012). Although Ginsberg et al. (2012) did not study the cost-effectiveness of clinical breast examination or other awareness raising programs, they acknowledge less expensive means of early detection in limited resource settings could be cost-effective in LMICs. When modeling the expected outcomes of such strategies - though based on limited evidence - Zelle et al. (2012) find that CBE screening and mass media awareness raising interventions indeed appear cost-effective in Ghana.

Although mammography interventions can be considered cost-effective, their total annual costs (budget impact) are high and may therefore not be appropriate for wide scale implementation.

If the necessary resources are not available both countries could choose to lower coverage levels or implement interventions with comparable ACERs (buying health just as efficiently) but with a lower budget impact. For Costa Rica, our analysis shows the most cost-effective option for expanding the current breast cancer services would be a CBE screening program combined with treatment of all stages. The yearly costs of this program are about US\$12 million. In 2009, the per capita health expenditure in Costa Rica was US\$660 (10.3% of GDP) (The World Bank Group, 2013c). With a population of approximately 4.5 million, implementing a CBE screening program would add US\$2.82 to this amount (0.43% increase). Although this

increase may seem feasible, the implementation and effectiveness of this program is highly dependent on the availability of human resources and the capacity of the healthcare system to refer and treat all new-found cases (Pisani et al., 2006; Miller et al., 2008; Anderson et al., 2011). Also, if the implementation of a CBE screening program would be unfeasible, MAR could be an interesting option as it is slightly less cost-effective but has a smaller yearly budget impact (US\$10 million). Yet, the very limited evidence on MAR's effectiveness requires our estimates to be interpreted with caution. Implementing a screening program for which the evidence base is stronger (e.g. mammography for women between 50-70 years of age) could be recommended if the yearly costs of US\$16 million are affordable. Mammography screening in age group 40-70 costs much more (about US\$21 million) and is therefore less economically attractive.

The Mexican MoH already decided to start increasing the use of the available infrastructure and mammography equipment for the population most at risk (women 50 to 70 years old and women with more than two risk factors). The gradual expansion will give enough time to train the required human resources. From our analysis the yearly costs of a mammography screening program for women 50-70 years of age at 95% coverage eventually would be US\$310 million per year, a threefold increase over the current situation. Next, once a reasonable increase on coverage would be reached the Mexican MoH plans to increase the coverage rate to women between 40-49 years of age (Fernández, June 8th, 2012). According to our estimates the yearly costs of implementing such a program would be US\$422 million. With approximately 110 million inhabitants and a per capita health expenditure of US\$525 in 2009 (6.43% of GDP) (The World Bank Group, 2013c), implementing these programs would add US\$2.82 (0.54% increase) and US\$3.84 (0.72% increase) respectively to the per capita health expenditure.

However, our analysis shows that perhaps strengthening actual MAR or CBE screening programs to be a more attractive first step in improving breast cancer services from an economic perspective. With yearly costs of US\$165 and US\$260 million if started from zero, the strengthening of existing programs is more affordable and more politically feasible as it would represent modest increases to existing budgets.

One of the principal questions we received from policy makers in both Costa Rica and Mexico concerned the addition of Trastuzumab to the treatment regimens. In Costa Rica we were asked to estimate the impact of implementing HER2/neu+ tests and prescribing Trastuzumab to those patients who have overexpression of this gene. As data on the proportion of patients with overexpression of the HER2/neu+ gene were not available, it was jointly decided to assume 30% of the breast cancer patients to have overexpression of the HER2/neu+ gene and to be eligible for Trastuzumab (Slamon et al., 2001). As a result of adding Trastuzumab, we estimate

Costa Rica can avert between 230 – 270 extra DALYs per year at an additional cost of approximately US\$7 million per year. For Mexico we obtained the actual proportion of patients receiving Trastuzumab in IMSS. Here the health gains comprise between 2,800 and 3,400 extra DALYs per year averted and the additional costs fall between US\$45 – 51 million. It is worth noting that in Mexico Trastuzumab is already provided as part of the treatment for all eligible women in stages I to IV. Our analysis shows the addition of this bio-pharmaceutical to increase the cost of treatment of stages I to IV by more than 48%, generating the need of developing public policies focused on negotiating price reductions that can contribute to mid- and long-term financial sustainability. The use of tools as the ones presented in this paper can provide technical evidence on the benchmark price that the Mexican health system could use in negotiations considering the threshold of one times the GDP per capita.

The limitations regarding the model are essentially the same as those reported in previous studies (Groot et al., 2006; Zelle et al., 2012). First, as evidence on the effectiveness of awareness raising, CBE and mammography screening in Costa Rica and Mexico were absent, we relied on the same model approach as used by Zelle et al. (2012). Second, when calculating unit costs for Mexico we did not account for the mark up of transportation costs (as generally recommended by WHO-CHOICE) and did not include the costs of facilities. Including these costs would have probably resulted in slightly higher unit costs. Third, we did not adjust the disability weights in those scenarios in which Trastuzumab was added because we did not find robust evidence on the impact of Trastuzumab on disability weights/quality of life values for breast cancer in each of the four stages. Because we had seen in the palliative care scenarios that changing the DWs had a minimal impact on the results, we decided against adding something of low quality and limited impact. Fourth, there is little evidence that Trastuzumab has a positive effect on overall survival in early stages. As one of the few references Smith et al. (2007) provide evidence that women with early stage breast cancer experience a better overall survival with Trastuzumab than without. Given the local practice and policy interest of including Trastuzumab in early stages, we used this as the basis of our case fatality rates. Fifth, for this study we spoke to the oncologists, radiologists and surgeons that we had access to. With that our interviews focused on the areas of the capitals of both countries, i.e., San José and Mexico City. We acknowledge a representative sample covering a wider geographic area would have been desirable. Finally, in adopting a health care perspective we did not take into account travel and opportunity costs. Including these costs would probably have increased costs generally. Our general conclusions remain the same although the ranges of several ACERs are overlapping. The limitations fit

within the overall goal of WHO-CHOICE which is to provide general indications of cost-effectiveness, i.e., not precise estimates of specific interventions.

In summary, for improving their current breast cancer control programs, our analysis suggests that both Costa Rica and Mexico would benefit from implementing strategies that advance early detection. For these countries, a mass-media awareness raising program and/or a CBE screening program coupled with treatment of all stages and careful monitoring and evaluation could be feasible options. If these strategies are implemented, the provision of breast cancer diagnostic, referral, treatment and, when possible, basic palliative care services is essential and should be facilitated simultaneously.



# Chapter 7

## Equity in Ghanaian Breast Cancer Treatment Outcomes: A modeling Study in Komfo Anokye Teaching Hospital

Forthcoming as:

Niëns LM, Nyarko KM, Zelle SG, Jehu-Appiah C, Rutten FFH. "Equity in Ghanaian Breast Cancer Treatment Outcomes: A modeling study in Komfo Anokye Teaching Hospital"

*The Breast Journal - Letter to the editor.*



**ABSTRACT**

With more and better health care services becoming available in Ghana, the equitable distribution of health outcomes becomes more important. In this study, we analyze which socio-economic groups benefit most from available breast cancer services in Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana. Using a mathematical model we estimate differences in Disability Adjusted Life Years (DALYs) averted between SES-groups. Although KATH patients from higher quintiles generally had a more favorable stage distribution, and thus avert more DALYs than those from lower quintiles, this difference was very small. Yet, compared to patients not receiving treatment at all, the number of DALYs averted by our sample was significant. The fact that over 75% of the patients presented with late stage disease begs the question if people actually have adequate information about breast cancer. It seems that equity in Ghanaian breast cancer care will benefit more from increasing awareness of breast cancer (symptoms) and treatment services to patients who currently do not seek nor receive care.

## 7.1 INTRODUCTION

Breast cancer is the most common cancer among women worldwide. Each year it is diagnosed in over 1 million women and accounts for 400,000 deaths (Groot et al., 2006). Although incidence rates are higher in high-income countries, low- and middle-income countries (LMICs) account for the majority of breast cancer deaths also because in LMICs the mortality-to-incidence ratio is much higher (Parkin et al., 2005). This problem is likely to get worse as changing lifestyles and improvements in sanitation and management of infectious diseases will probably result in higher breast cancer incidence rates in LMICs. Incidence levels have been rising at 5% per year in some developing areas (International Agency for Research on Cancer Working Group on the Evaluation of Cancer-Preventive Strategies, 2002; Stewart & Kleihues, 2003; Ferlay et al., 2004).

In high-income countries much progress has been made in reducing breast cancer mortality (Parkin et al., 2001; Parkin et al., 2005). However, the benefits of decreased mortality are not distributed equitably over the population. Studies have revealed differences in breast cancer burden by race (Ward et al., 2004), urbanization (Joseph Sheehan et al., 2004), insurance status (McDavid et al., 2003; Wilf-Miron et al., 2010) and socio-economic status (SES) (Lantz, 2006). Defined as “the absence of avoidable or remediable differences among groups of people, whether those groups are defined socially, economically, demographically, or geographically” the equitable provision of health care is an important goal of the World Health Organization (World Health Organization, 2010). Besides the efficient use of resources when implementing health care programs, the question of how to ensure that their benefits are equitably distributed is thought to be equally important in LMICs (Magrath & Litvak, 1993; Pal & Mittal, 2004).

Equity in breast cancer care has been studied in high-income countries (McDavid et al., 2003; Joseph Sheehan et al., 2004; Ward et al., 2004; Lantz, 2006), but less so in middle-income countries (Charry et al., 2008; Velasquez-De Charry et al., 2009), and almost not at all in low-income countries. The relatively heavy data requirements for carrying out equity studies in combination with non-existing (national) cancer registries in many low-income countries may account for this (Parkin et al., 1999; Parkin et al., 2005).

This study tries to address this void in the literature and assesses equity of treatment outcomes of breast cancer care in Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana. We investigated whether lower SES patients in KATH present with more advanced disease and have worse health outcomes.



The paper is structured as follows. First, the Ghanaian health care system and its equity profile are shortly discussed. Second, our data collection and methods are described. Next, we present and interpret our results.

## 7.2 EQUITY AND BREAST CANCER TREATMENT IN GHANA: THE ROLE OF HEALTH INSURANCE

In Ghana, most breast cancer care is provided in the two academic hospitals -i.e., Korle Bu Teaching Hospital in Accra and Komfo Anokye Teaching Hospital in Kumasi- and the Peace and Love Hospital, a specialized breast clinic located at Oduom, Ashanti Region and Accra. The Ghanaian Health Service (GHS) does not have a national early detection program for breast cancer in place (Ohene-Yeboah & Adjei, 2012; Zelle et al., 2012) but several non-governmental organizations (NGOs)<sup>1</sup> work on raising awareness and explain self-breast examination to women in remote villages. In the three aforementioned institutions mammography is available for diagnostic reasons. Treatment of patients in general involves a lumpectomy or mastectomy, endocrine therapy and (if required) chemo- and/or radiotherapy. Due to lack of resources diagnosing HER2/neu receptor status often is not possible (Ohene-Yeboah & Adjei, 2012). For the same reason most patients are not treated with expensive monoclonal antibodies like Trastuzumab.

In March 2004 access to the GHS was improved when the Ghanaian Government officially launched the Ghanaian National Health Insurance System (NHIS). It replaced a cash-and-carry system whereby patients had to pay for health services out-of-pocket (Sarpong et al., 2010). With the indigent and the poor exempt from paying premiums (Jehu-Appiah et al., 2010), within four years over 55% of Ghana's population was registered (Jehu-Appiah et al., 2011). While a real accomplishment, evidence suggests that enrollment among the poor, both urban and rural, is rather low (Asante & Aikens, 2007; Health Sector Advisory Office, 2008; Jehu-Appiah et al., 2010; Jehu-Appiah et al., 2011). In a report written for the Ghanaian Ministry of Health Asante and Aikens note that:

*“the association between NHIS card holders and socio-economic status is significant ( $p < 0.0001$ ) with respondents being more likely to hold an NHIS membership card if they belong to richer quintiles.” (Asante & Aikens, 2007)*

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1. Two NGOs working on Breast cancer in Ghana are: “Mammocare” and the “Sister Support Network”.

As Ghana does not have a national cancer registry (yet) and knowledge of cancer patterns is mostly “based on hospital series collected by clinicians and pathologists” (Parkin et al., 1999; Parkin et al., 2005) in this paper we study whether the outcomes of breast cancer treatments in KATH are equitably distributed across income quintiles.

### 7.3 MATERIALS AND METHODS

#### Data

Between November 2009 and January 2010 we assembled 200 records of breast cancer patients that had received or were still receiving treatment at KATH in Kumasi. All patients diagnosed between January 1st 2008 and December 31st 2009 were eligible for the study. In 2008 and 2009 respectively 149 and 140 breast cancer patients were seen. The non-response of 89 was due to the inability to trace patients, lack of consent and death at the time of study.

To determine differences in treatment outcomes, we collected data on breast cancer stage at diagnosis. The breast cancer's stage helps medical practitioners to estimate the prognosis of the disease and decide on treatment options. It is often done according to the general principles of the American Joint Committee on Cancer (AJCC) staging system which takes into account the size of the tumor, the number of positive regional lymph nodes and possible metastasis (Fleming et al., 1997). The AJCC staging system includes both a clinical and a pathological classification. Whereas clinical classification “is based solely on evidence gathered before initial treatment of the primary tumor” (Singletary & Conolly, 2006), pathological classification “takes into account evidence obtained from surgery and from detailed pathologic examination of the primary tumor, lymph nodes, and distant metastases” (Singletary & Conolly, 2006). Although pathology services in Ghana are becoming more available, local investigators were only able to retrieve the clinical stage of 90 patients (Stalsberg et al., 2008). The characteristics of the 110 patients for which they could not identify the clinical stage were very similar to those 90 for which they could.

#### SES

Our patients' SES was estimated from their expenditures on: clothing, education, food, funerals, garbage collection, health, housing, lighting, remittances to other households, sanitation (toilet), transportation, wages and water. These were retrieved through face to face interviews of patients receiving treatment at the time of the study and telephone based interviews for those who had being diagnosed

with breast cancer but were at home during the time of the study. For the interviews, through which we also identified insurance status, we used a questionnaire as developed and validated by Jehu - Appiah et al. (2011). The SES-quintiles were constructed by ranking our sample by household expenditures. Since we had both SES and breast cancer stage for 90 patients, each quintile contained 18 patients. The cut-off points used to assemble our quintiles equal the maximum monthly household expenditure figures of every eighteenth patient.

### **Model**

To see if treatment outcomes differed between patients, in line with other equity studies (Kongsri et al., 2011; Rahman et al., 2011; Ruhago et al., 2011), we calculated the averted Disability Adjusted Life Years (DALYs) per SES group. The DALY is a summary measure of population health which is "calculated as the sum of the years of life lost due to premature mortality in the population and the equivalent 'healthy' years lost due to non-fatal health conditions" (Tan-Torres Edejer et al., 2003). Hence, to calculate DALYs we need information on case fatality rates (CFs) and quality of life estimates or disability weights (DWs). It follows that averting DALYs equals gaining health. The effects of breast cancer interventions for each of the four cancer stages in Ghana have been calculated by Zelle et al. (2012) who used an improved mathematical model as initially developed by Groot et al. (2006). Based on WHO-CHOICE methodology (described elsewhere (Tan-Torres Edejer et al., 2003; Groot et al., 2006)) this model uses CFs from Bland et al. (1998) and estimates DWs from various other studies (de Koning et al., 1991; Murray & Lopez, 1996.; Launois et al., 1996; Norum, 1999). In the model, patients in each of the four AJCC breast cancer stages receive the treatment currently given in Ghana and are exposed to stage specific CFs and DWs. For each of the five quintiles in our sample, we calculated the DALYs averted by entering a quintile-specific stage distribution in the model. In line with WHO-CHOICE methodology DALYs are discounted at an annual rate of 3% (Tan-Torres Edejer et al., 2003). DALYs averted are calculated without age weights as to not distort the total DALYs averted by elderly women receiving a lower weight than middle aged women (Tsuchiya, 1999).

Patients not receiving treatment do not avert DALYs associated with breast cancer control. They experience the natural progression of the disease and therefore have much higher case fatality rates. As such, in our analysis, the SES-quintiles and how their different stage distributions affect the number of DALYs averted, will be compared with the population not receiving treatment. Hence, we combine access to treatment and SES with our analysis of the breast cancer stage at presentation of 90 patients in KATH.

## 7.4 RESULTS

Table 1 shows relevant characteristics of our patient sample. Over 95% of our 90 patients had health insurance. Although the average age (54.67 years) and number of children (4.00) were higher in the 1st quintile than in the other quintiles (45.78 – 50.28 years and 2.80 – 3.93 children) these differences were not statistically significant. The stage distribution of our total sample we find to be slightly different from those reported by Ohene-yeboah and Adjei (2012) (also from KATH), Zelle et al. (2012) (from Korle Bu Teaching Hospital sample) and Groot et al. (2006), i.e., the total proportion of patients in low (I & II) and high (III & IV) stages is similar in all distributions.<sup>2</sup> University educated patients were only found in the 4th and 5th quintile and the monthly average household expenditures of the latter (Ghana Cedi (GHC) 379) were more than three times those of the 1st quintile (GHC 124) and more than twice those of the 2nd quintile (GHC 177). Comparing these average household expenditures with those found in the latest round (5th, in 2005-06) from the Ghana Living Standards Survey (GLSS, a nationally representative household survey) showed those from the KATH sample to be higher. However, applying the consumer price index (CPI) from the World Bank's Development Indicators to correct for price increases between 2006 and 2010 nullified these differences (Table 2) (The World Bank Group, 2013c). Thus, the patients in our sample have similar expenditure patterns for each quintile as the population of Ghana as a whole.

The stage distributions and DALYs averted per patient for each of the SES-quintiles are presented in Table 3. Stage distributions between the 1st, 2nd, and 3rd SES-quintiles are very similar with no or only 5.6% of patients presenting at the hospital with stage I disease. In the 4th quintile, 27.8% of the patients present in stage I. Hence, whereas overall over 75% of the patients presented with late stage disease (III or IV) in the 4th quintile this is just 50%. In the 5th quintile all patients presented in stage II or III. Although more favorable for the higher SES-groups, overall stage distributions are not significantly different (p-value Fischer's exact test: 0.083). From our analysis it results that the 18 patients from our 1st quintile in KATH, would avert 19.50 DALYs compared to no treatment (Table 3). This is an average of 1.084 DALYs averted per patient. Assuming the stage distribution of all patients equals that of the 5th quintile leads to 20.93 DALYs averted, or an average of 1.163 DALYs averted

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2. For stages I through IV the following distributions were reported:

- Ohene-Yeboah: 3.6% - 11.2% - 70.0% - 15.2%
- Zelle et al.: 2.3% - 20.5% - 50.0% - 27.3%
- Groot et al.: 9.4% - 14.2% - 58.0% - 18.4%

**Table 1:** Descriptive Statistics of SES-quintiles

Variable	SES						
	I	II	III	IV	V		
<b>Age</b>							
Minimum	30	39	26	35	29		
Maximum	85	70	86	74	78		
Mean	54,67	48,72	45,78	50,28	48,94		
Std. Deviation	17,71	8,50	15,18	9,49	14,04		
<b>Parity</b>							
Minimum	2	1	1	0	1		
Maximum	6	6	7	10	10		
Mean	4,00	3,67	2,80	3,50	3,93		
Std. Deviation	1,77	1,75	1,81	3,44	2,52		
<b>Monthly household expenditure</b>							
Minimum	60,00	158,00	202,50	236,00	287,00		
Maximum	158,00	202,00	231,00	284,00	556,00		
Mean	123,84	176,97	215,46	259,81	379,42		
Std. Deviation	28,25	13,28	9,20	14,13	90,08		
<b>Marital Status</b>							
married	9	9	8	12	10		
single	1	2	3	1	1		
widowed	3	6	6	0	0		
divorced	5	1	1	5	6		
missing	0	0	0	0	1		
<b>Total (N)</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>		
<b>Health Insurance</b>							
Yes	18	17	17	17	17		
No	0	1	1	1	1		
<b>Total (N)</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>		
<b>Education Level</b>							
none	11	4	2	4	1		
elementary	7	11	9	5	8		
secondary	0	3	7	7	8		
university	0	0	0	1	1		
missing	0	0	0	1	0		
<b>Total (N)</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>		
<b>Breast cancer stage</b>							
I	0	0	1	5	0	6	6,67%
II	2	3	2	4	4	15	16,67%
III	13	13	13	7	14	60	66,67%
IV	3	2	2	2	0	9	10,00%
<b>Total (N)</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>18</b>	<b>90</b>	<b>100,00%</b>

**Table 2:** Monthly average household expenditure

SES Quintiles	Patient sample KATH - 2010	Ghana Living Standards Survey (GLSS) 2005-06	GLSS 2005-06 brought to 2010 with CPI
I	GHC 124	GHC 68	GHC 117
II	GHC 177	GHC 104	GHC 176
III	GHC 215	GHC 131	GHC 222
IV	GHC 260	GHC 162	GHC 276
V	GHC 379	GHC 239	GHC 407
<b>Total</b>	GHC 231	GHC 160	GHC 272

per patient. DALYs averted for the other three quintiles fall between these values. Patients in the 4th quintile had the most favorable stage distribution (27.8% and 22.2% in stage I and II respectively) and averted on average 1.10 DALYs. The patients in the 4th quintile avert less DALYs than those from the 5th because the effects are discounted at a rate of 3%. Discounting corrects for the fact that in general society prefers to receive benefits sooner rather than later. Hence, future effects receive less weight and are scaled down to their present value. Because patients in earlier stages avert most of their DALYs in the future the present value of their DALYs averted is lower.

**Table 3:** Average number of DALYs averted for five SES-quintiles in KATH treated for breast cancer.

SES quintiles	Stage distribution <sup>a,b</sup>				DALYs per patient no age weight but discounted at 3% per year <sup>c</sup>	DALYs per patient no age weight undiscounted <sup>c</sup>
	Stage I	Stage II	Stage III	Stage IV		
I	0.0%	11.1%	72.2%	16.7%	1.08	1.56
II	0.0%	16.7%	72.2%	11.1%	1.11	1.61
III	5.6%	11.1%	72.2%	11.1%	1.10	1.61
IV	27.8%	22.2%	38.9%	11.1%	1.10	1.77
V	0.0%	22.2%	77.8%	0.0%	1.16	1.71

<sup>a</sup> stage distributions were not significantly different – Fisher’s Exact Test: 0.084 (2-sided)

<sup>b</sup> assumed to be equal to KATH population

<sup>c</sup> compared to no treatment at all.

## 7.5 DISCUSSION

We combined expenditures and clinical breast cancer stage for 90 patients in Komfo Anokye Teaching Hospital in Kumasi, Ghana, with a cost-effectiveness model based on WHO-methodology, and studied the equity situation in KATH. Although we did find a trend of lower wealth quintiles having a slightly less favorable stage distribu-

tion, indicating that richer patients present themselves at the hospital sooner, the differences in DALYs averted between SES-quintiles in KATH were very small. Our results show that patients who could access KATH did not experience inequities in treatment outcomes. However, there are probably many breast cancer patients that cannot access breast cancer diagnosis and treatment. This has most likely to do with the lack of adequate information on breast cancer signs and symptoms (low awareness) and a poor treatment infrastructure (urban only) and referral system (van den Boom et al., 2004; Harford et al., 2011). Indeed, to improve breast cancer outcomes, ensuring that people present themselves at the hospital with early stage disease is paramount. The fact that in our sample over 75% of our patients still present at the hospital with late stage disease signals that there is an awareness problem. Shulman et al. (2010) show that in the US “mortality-to-incidence ratios decreased dramatically, even before the generalized use of mammography or adjuvant chemotherapy and antiestrogen therapy that commenced in the mid- to late 1970s”. US data on breast cancer survival before 1974 suggest that these improvements in breast cancer survival are due to breast education and awareness programs (Flannery & Sullivan, 1978; Jatoi et al., 2005). More recent work also advocates the increase of awareness, education and capacity at primary and community health care facilities in low-income countries like Ghana to address the ever increasing burden of breast cancer (Anderson, 2006; Anderson & Carlson, 2007; Collingridge, 2009; Kerr & Midgley, 2010; Harford et al., 2011). Furthermore, as treating early stage breast cancer is found to be less costly than late stage disease (Campbell & Ramsey, 2009), it comes as no surprise that Zelle et al. (2012) found a mass media campaign to increase awareness to be one of the most cost-effective interventions.

This study has some limitations. First, as we had a non-response of 89 patients and were able to retrieve clinical stage for 90 patients only, possible selection bias could affect the breast cancer stage at diagnosis and SES of our sample. If these 89 patients were of low-SES and this was correlated with a worse stage at diagnosis this might explain why we did not find significant differences between stage distributions. On the other hand, our sample's stage distribution differs only slightly from those found by other authors (Groot et al., 2006; Ohene-Yeboah & Adjei, 2012; Zelle et al., 2012). Also, we showed that although the large majority of our patients reside in the Ashanti region (one of Ghana's richest regions in the country's middle belt (Business Guide, 2011)) their SES is similar to that of the Ghanaian population. Second, the high insurance uptake of our patients, also in the poorer quintiles, was surprising as average household expenditures did not differ from the general population and previous studies in Ghana reported a strong relationship between income and health insurance uptake (Asante & Aikens, 2007; Health Sector Advisory Office, 2008; Jehu-Appiah et al., 2010; Jehu-Appiah et al., 2011). Upon further investigation our local

partners told us many people in Ghana only register with the NHIS once they get sick, which might explain the high insurance uptake in our sample (Nyarko, 2011). After registration it takes approximately 6 months before benefits can be claimed, however. Hence, although the received treatment at KATH is paid for out of pocket initially, for conditions which last longer (chronic), registering with the NHIS once confronted with sickness appears to be rational. Because we do not know which patients already had insurance upon reporting at the hospital we cannot answer the question if there is a positive relationship between insurance and treatment outcomes as was found in previous studies (McDavid et al., 2003). Furthermore, although all the patients in our sample received treatment, from interviews with doctors and local NGOs,<sup>3</sup> we know that numerous breast cancer patients in Ghana in fact do not. This may be attributed to the fact that breast cancer is a taboo for many in the Ghanaian population (Errico & Rowden, 2006). Another reason may be the geographical coverage of breast cancer services of approximately 10% (Zelle et al., 2012). As detailed information about the group of patients not receiving care is lacking, we cannot exclude this group to also encompass (some) people who have insurance. Of course, if a large percentage of the untreated in fact also has insurance then other barriers to access than financial may exist as well. In addition, as medical tourism is flourishing in Africa (Connell, 2006; Herrick, 2007; Helble, 2011), Ghana's richest people may go abroad for treatment, thereby not being part of our sample (Africa news, 2010). While our study shows the health outcomes in KATH are equitably distributed over the SES quintiles, it is too small for extrapolation to Ghana's total population (of breast cancer patients). Nonetheless, since KATH is one of the two breast cancer disease management centers in Ghana<sup>4</sup> (which see the vast majority of breast cancer patients, i.e., also those from Peace and Love hospital) we argue that the sample may provide a reasonable picture of current Ghanaian breast cancer patients. The fact that it contained a relatively low number of patients from other regions may signal access to services is hindered by low geographical availability of services as well. As Ghana is in the process of setting up a cancer registry, hopefully in the future some of these limitations may be addressed.

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3. "Mammocare" and the "Sister Support Network"

4. The other is Korle Bu Teaching Hospital in Accra



## 7.6 CONCLUSION

The fact that treating similar patients with the same intervention causes the outcomes to be the same is not new (Dignam et al., 1999; Blackstock et al., 2006). Inequity across those treated in Komfo Anokye Teaching Hospital with different SES appears to be limited. The fact that the large majority of our patients presented with late stage disease signals low awareness. Low geographical availability of breast cancer treatment services may hinder access too. As treatment of breast cancer is effective in averting DALYs, the best option to improve equity in Ghanaian breast cancer care is probably to improve awareness and access to care.

# Chapter 8

## Gendered Epidemiology: Sexual Equality and the Prevalence of HIV/AIDS in Sub-Saharan Africa

Based on:

Niëns LM, Lowery D. "Gendered Epidemiology: Sexual Equality and the Prevalence of HIV/AIDS in Sub-Saharan Africa."

*Social Science Quarterly* 2009 90(5): 1134-44.



**ABSTRACT**

Given that HIV/AIDS in sub-Saharan Africa is largely spread through heterosexual contact, there is marked variation in levels of gender equity across sub-Saharan African countries, and levels of gender equity are likely to influence both exposure to sexual practices that increase the likelihood of exposure to HIV and the efficacy of prevention programs, we hypothesize that levels of gender equity account for the levels of and changes in the prevalence of HIV/AIDS across sub-Saharan African countries.

We explore this hypothesis by first discussing the role of gender and several other contextual variables in the spread of HIV/AIDS. The resulting model is tested with regression analyses of both the level and change of HIV/AIDS in sub-Saharan African.

We find strong support for our hypothesis. This suggests that further policy attention be given to gender equity in combating HIV/AIDS.

## 8.1 INTRODUCTION

In explaining variations in levels of HIV/AIDS across countries, scholars have identified determinants that range from those that can be readily manipulated, such as adoption of programs to distribute condoms, to those that cannot be changed, such as a country's legacy of colonialism. Among the most interesting of these, we think, are those determinants that fall between these extremes of ease of manipulation. Of these, we think that perhaps one of the most interesting is the level of gender equity, an expectation that is driven by three hard facts about sub-Saharan Africa. First, HIV/AIDS in sub-Saharan Africa is largely spread through heterosexual contact (Akeroyd, 2004; UNAIDS, 2006). Second, there is marked variation in levels of gender equity across African countries (United Nations Development Program, 2012a). And third, levels of gender equity are likely to influence both exposure to sexual practices that increase the likelihood of exposure to HIV (Schoepf, 1988; Orubuloye et al., 1996) and the efficacy of prevention programs, such as the use of condoms (Kesby, 2004). We test the hypothesis that HIV prevalence is related to gender equity and then note policy implications of our findings.

## 8.2 THE GENDERED CONTEXT OF HIV/AIDS

HIV/AIDS in sub-Saharan Africa (henceforth simply Africa) is largely spread through heterosexual contact, with men largely responsible for the spread of the disease (Akeroyd, 2004; Halperin et al., 2008). And while, at the outset of the epidemic, the sex ratio of HIV/AIDS cases was almost equal, over time, data showed that infections among women increasingly outnumbered those in men (Akeroyd, 2004; UNAIDS, 2006). It seems plausible, then, that relationships between men and women influence each sex's exposure to the disease and opportunity to practice prevention. Therefore, it is likely that gender issues bearing on those relationships are an important factor in explaining variations in the course of the epidemic.

Gender matters in several ways. At the broadest level, Connell (1987) has argued that such gender differences can be explored by looking at the structures of labor, power, and cathexis that determine the relationships between men and women in a society. The labor factor concerns such variables as the organization of housework and childcare, unequal wages, the division between unpaid/paid work, and so on. The second factor has to do with the nature of authority, control, and coercion in a society. Cathexis refers to those relationships subject to desire and desirability, jealousy, distrust, and emotional relationships with children. Wingood and DiClemente (2000) applied Connell's framework to the AIDS epidemic to assess how variation

in these factors influenced women's vulnerability to HIV. Until the late 1990s, policies dealing with HIV/AIDS were based on the assumption that the individual had total control over his or her behavior. Still, such policies were more often than not aimed at women (Akeroyd, 2004). But in promoting these programs, Wingood and DiClemente (2000) noted that the kinds of differences in power noted by Connell that heighten women's vulnerability to AIDS were simply not taken into account. This failure had significant consequences for the effectiveness of prevention and treatment programs. Indeed, according to Baylies and Burja (1995), it is primarily gendered inequality that puts both men and women at risk. As a result, policies that focus on gender issues may be a fundamental tool in fighting HIV/AIDS and a precondition for more effective treatment and prevention programs.

More specifically, culturally, legally, and economically, females are often not equal to men, and these differences may foster higher HIV prevalence among women. Because of their subordinate position, women all too often do not have the final say when it comes to cultural violence and sexual practices associated with the spread of HIV/AIDS. Practices in which a woman's vagina is damaged, for example, circumcision, and intra-vaginal substances that dry and tighten the vagina before sexual intercourse, increase the risk of becoming infected (Schoepf, 1988; Orubuloye et al., 1996; Mgalla et al., 1997). Further, the belief that sex with a virgin will cure AIDS is common in Africa (Schoepf, 2004). This puts young women at risk of rape. The latter is a manifestation of power over the powerless and also regularly occurs in settings of conflict (see footnote 1). But it should be clear that these specific forms in which exposure to HIV is heightened are consistent with Connell's broader notion of gendered power structures.

Micro-level research (Kesby, 2004), as well as conventional survey evidence (McFadden, 1992; Meursing, 1997; Akeroyd, 2004), also supports the idea that gender matters in fighting HIV. Mgalla, Wambura, and de Bruyn, for example, argue that different norms apply to men and women when it comes to sexual activity, norms that decrease women's negotiation power regarding condom use and faithfulness (Mgalla et al., 1997). Still, it is not clear that differences in sexual practices associated with exposure to HIV/AIDS and the efficacy of prevention practices are sufficient to account for the very substantial variation across countries and over time in levels of HIV/AIDS. However, based on the foregoing, we hypothesize that the LEVEL OF GENDER EQUALITY in a country is negatively related to HIV prevalence. HIV levels should decrease across countries as women become empowered and more equal to men. Further, the growth rate of HIV/AIDS should be associated with changes in the level of gender equity across countries.

Obviously, gender is not the only thing that might plausibly influence cross-national variation in HIV/AIDS levels.<sup>1</sup> Based on prior work, and recognizing the complexity of the causal processes at work, our model includes controls for ECONOMIC DEVELOPMENT (Shelton, 2005; McIntosh, 2006), ECONOMIC GROWTH (Brown, 2004), EDUCATION (Schoepf, 1988; UNAIDS, 2006), and how well the HEALTH-CARE system functions (Schoepf, 1988; Hunt, 1989; UNAIDS, 2006). The final factor is RELIGION, which is thought to influence vulnerability to HIV in several ways (Noell et al., 1993; Mgalla et al., 1997; Lagarde et al., 2000; Mbulaiteye et al., 2000; Bailey, 2001). Still, prior research (Gray, 2004; Oponng & Agyei-Mensah, 2004) has found that the percentage of Muslims in a country negatively predicted HIV prevalence.

### 8.3 TESTING THE HYPOTHESIS

#### Data and Operationalization

We test two sets of models using separate dependent variables. The dependent variable in the first set of models is HIV PREVALENCE RATES as published by UNAIDS (UNAIDS, 2006).<sup>2</sup> In 2003, HIV prevalence rates varied from a low of 0.20 percent in Mauritius to a high of 32.40 percent in Swaziland, with a mean of 7.29 percent. Separate estimates were generated for each year from 2000 to 2005, with the

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1. We also examined a number of other variables that might be expected to influence HIV/AIDS prevalence. However, none generated significant estimates in any of the models we examined, nor did their exclusion discernibly influence the estimates of the variables retained in the models. These included level of VIOLENCE (UNAIDS, 2006; Akeroyd, 2004; Oponng and Agyei-Mensah, 2004) as measured by the number of refugees residing in a country as a percentage of its total population (UNHCR, for number of refugees; World Bank, for total population—both for 2000–2005 period), form of government (Przeworski, Alvarez et al., 2000), as measured by the Freedom House Index (Freedom House, data for 2000–2005), level of NGO ACTIVITY (Marmot, 2004), as measured by the number of NGOs engaged in HIV/AIDS related activities in a country, and the legacy of COLONIAL EXPERIENCES on AIDS prevalence, as measured with dummies for the four largest colonizers in sub-Saharan Africa. We also examined participation in THE SOUTHERN AFRICAN DEVELOPMENT COMMUNITY (SADC) with a dummy for its 14 member counties. SADC issued in July 2003 a declaration on HIV/AIDS indicating a joint anti-AIDS effort. None of these variables generated discernible results. We also examined Lieberman's finding that the ethnic fractionalization of a country influences HIV/AIDS (Lieberman, 2007), but we assume that this effect is captured by the more proximate variable of health spending.
  2. We use all sub-Saharan Africa countries as defined by UNAIDS. UNAIDS recently changed its methodology in its surveys of HIV prevalence rates, effective in the 2007 report. Thus, we use the 2006 report for consistency across the 2000–2005 period.

dependent and independent variables measured in the same year or, in very few cases (noted in the text), the most temporally proximate value of the independent variable or as noted for intentionally lagged variables. All produced strikingly similar results.<sup>3</sup> We present, therefore, only the models for 2000 and 2005.<sup>4</sup> The second set of models employ as a dependent variable CHANGE IN HIV PREVALENCE as measured by change in a country's HIV prevalence between 2000 and 2005. Change in HIV prevalence rates from 2000 to 2005 varied from a low of -11.70 percent in Botswana to a high of 8.15 percent in Swaziland, with a mean change of -1.56 percent. Several specifications of the change score model were tested, including several with virtually all combinations of baseline 2000 and change from 2000 to 2005 values of the independent variables. Again, all the models produced similar results with few estimates discernibly different from zero. We present, therefore, only a simple change score model including the baseline value of AIDS prevalence in 2000 as a control to assess whether there is a ceiling/floor effect or inertia in infection levels that make change more or less likely, the baseline and change score values of our measure of gender equity, and the 2000 baseline value of the other independent variables.

To measure the critical GENDER variable, we used the Gender-Related Development Index (GDI) from The U.N. Development Program (UNDP) development reports. This index is based on measures of average achievement across three basic dimensions captured in the human development index. These are a long and healthy life (based on life expectancy at birth), knowledge (based on the adult literacy rate and the combined primary, secondary, and tertiary gross enrollment ratio in schools), and a decent standard of living (estimated earned income is used). The GDI is calculated in three steps. First, for each dimension, indices for both males and females are calculated. Second, the results are combined in one index that penalizes differences in achievement between men and women. Finally, through combining the three indices, the GDI is calculated.<sup>5</sup> We used the index values from the 2000–2005 UNDP development reports (data from 1998/2003). The 2003 report values of the Gender-

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3. We also examined a number of other potential lags in the analysis. All produced quite similar results. In perhaps the most telling of these, Models 4, 5, and 6 in Table 1, which use 2005 values for the dependent variable, were re-estimated using not the most proximate lags of the independent variables, but the much longer lags used in Models 1, 2, and 3 of Table 1. Essentially identical results to those presented in Table 1 were obtained. The results are also robust to potential violations of the normality assumption and outliers.
  4. Number of observations for the means vary slightly because of missing data.
  5. See HDR (2005:343), available at: [http://hdr.undp.org/en/media/HDR05\\_complete.pdf](http://hdr.undp.org/en/media/HDR05_complete.pdf).

Related Development Index varied from 0.27 in Niger to 0.78 in Mauritius, with a mean of 0.45. From the 2000 to 2005 reports, the values of the index varied from -0.17 in Swaziland to 0.10 in Equatorial Guinea, with a mean change of under 0.01.

Obviously, the GDI on its own terms is best viewed as a general development measure, albeit one heavily weighted for differences in gender equity. To use the GDI as a valid measure of gender equity, then, we must control for its underlying components reflecting development more generally.

This is especially true since the two most key elements of the GDI reflect two of our most plausible rival explanations, those associated with economic development and level of education. To both distill a more valid measure of gender equity and generate interpretable estimates to test these rival hypotheses, we include separate measures of economic development and level of education in the model as controls. Once we statistically control for level of economic development and level of education, the GDI estimate should indicate the unique impact on HIV/AIDS of gender inequality in development. The UNDP reports provided the indicators for the variable ECONOMIC DEVELOPMENT: the gross domestic product per capita per year based on purchasing power parities (GDP per-capita/PPP). Values of this measure in 2003 varied from 548 in Sierra Leone to 19,780 in Equatorial Guinea, with a mean of 2,711.<sup>6</sup> LEVEL OF EDUCATION is operationalized by the education index from UNDP development reports, which is based on the adult literacy rate and the combined gross enrolment ratio for primary, secondary, and tertiary schools. We used the education indices from the 2000 through 2005 reports (data from 1999/2004). The values in the 2003 report varied from 0.16 in Burkina Faso to 0.81 in South Africa (mean = 0.55).

The importance a government attaches to its HEALTH-CARE SYSTEM is measured by general government spending on health as a percentage of total government expenditure in 1998–2003 (World Health Organization, 2012c).<sup>7</sup> Health-care expenditures as a proportion of total government expenditures varied from a low of 2.00 percent in Burundi in 2003 to a high of 17.60 percent in Liberia, with a mean of 8.97 percent. Data on RELIGION are taken from the 2006 Freedom House survey. Percent

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6. Change in the values of the economic development measure varied from -999 to 15,834, with a mean of 811. The comparable values for education were -0.12, 0.17, and 0.02. For health-care expenditures, the values were -7.20, 6.70, and 0.42.

7. There is, however, the possibility of collinearity between health-care spending and level of economic development. But the fact that we were able to generate statistically discernible estimates for both in several of the models suggests that collinearity is not so severe as to preclude valid inferences about independent influences.



Muslim varied from 1.00 percent in Zimbabwe in 2000 to 98.00 percent in Comoros, with a mean of 38.16.<sup>8</sup>

There are four final things to note about the estimating models. First, our hypotheses about economic development are complex given that they point to the effects on AIDS prevalence of both the level and rate of change in GNP. We found no evidence of the latter in our models (not reported) of change in AIDS prevalence. But in the first, static set of models, we include the economic development variables as a second-order polynomial to assess whether the effects of wealth on AIDS prevalence vary across values of wealth or whether they have a curvilinear relationship with AIDS prevalence. Second, given potential collinearity between the gender development index and percent Muslim,<sup>9</sup> we examine models both including and excluding percent Muslim. Third, we employ one-tailed tests for our gender variables given our strong expectations about their relationship with AIDS prevalence. And fourth, given few observations and potential collinearity, we employ somewhat more relaxed criterion levels.

## 8.4 RESULTS

Table 1 presents the results for the models employing the 2000 (Columns 1 through 3) and 2005 (Columns 4 through 6) values for AIDS prevalence. Starting with the control variables, the education coefficient is positive and significant across all models. In contrast, while the estimates for per-capita spending on health generated positive estimates in all cases, only those in the 2005 models were discernibly different from zero, albeit only modestly so. The percentage of the population that was Muslim generated a negative estimate in all four of the models in which it was included, although none was significant. More importantly for our purpose, the inclusion of percent Muslim does not seem to diminish the estimates for our key independent variable – the GDI. Indeed, the estimates for GDI are greater in magnitude in the models including percent Muslim: Models 2 and 3 for 2000 and 5 and 6 for 2005. The inclusion or exclusion of percent Muslim had, however, a strong impact on the

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8. We also looked at Africa's three most widespread religions—Islam, Christianity (Catholic and Protestant), and indigenous beliefs—using separate dummies, but with null results. There was no substantively meaningful variation in percent Muslim over the period we examined. We examine only static measures, therefore, of the religion variable.

9. 10The correlations between GDI and percent Muslim over recent years were not as strong as some might expect, ranging from -0.45 in 1998 to -0.34 in 2001.

**Table 1:** OLS Test of Determinants of HIV/AIDS Prevalence, 2000 and 2005

Independent Variable	2000 HIV/AIDS Prevalence			2005 HIV/AIDS Prevalence		
	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Gender Index	-59.220### (25.007)	-121.754### (28.482)	-137.868### (21.713)	-60.863### (19.906)	-77.532### (23.159)	-83.332### (15.127)
Economic Development	0.000 (0.001)	0.002*** (0.001)	0.010*** (0.002)	0.000 (0.000)	0.002** (0.001)	0.009*** (0.001)
Economic Development Sq.	–	–	-0.007*** (0.002)	–	–	-0.006*** (0.001)
Education Index	55.764*** (12.810)	66.525*** (14.572)	65.174*** (10.950)	53.548*** (10.189)	42.529*** (13.469)	42.226*** (9.776)
Per Capita Health Spending	0.468 (0.379)	0.381 (0.284)	0.161 (0.219)	0.903** (0.343)	0.796* (0.397)	0.520* (0.264)
Percent Muslim	–	-0.017 (0.043)	-0.022 (0.032)	–	-0.052 (0.059)	-0.043 (0.039)
Constant	0.499	19.744	21.649	-4.576	8.688	4.943
R-Sq.	0.434	0.659	0.816	0.529	0.575	0.828
N	36	28	28	35	26	26

### =  $p < 0.01$ , one-tailed test. \* =  $p < 0.10$ ; \*\* =  $p < 0.05$ ; \*\*\* =  $p < 0.01$ , two-tailed; values between brackets are standard errors.

coefficients for economic development. That is, the estimates for per-capita GDP were not significant in Models 1 and 4, which exclude percent Muslim, but they were positive and highly significant in the remaining models, suggesting that AIDS prevalence increases as nations become wealthier. But the inclusion in Models 3 and 6 of the squared value of per-capita GDP in the second-order polynomial specification of the impact of economic development modifies this conclusion to some degree. That is, the negative and significant estimates for the squared values of per capita GDP indicate that the generally positive impact of wealth on AIDS declines as nations become wealthier. What of our key explanatory variable –the GDI? As seen in the shaded portion of Table 1, GDI produces highly significant, negative estimates across all the models. As expected, countries with greater levels of gender equality had significantly lower levels of AIDS in both 2000 and 2005.

Table 2 employs change in HIV/AIDS prevalence from 2000 to 2005 as our dependent variable. The model includes the baseline value of AIDS in 2000 to control for possible ceiling or floor effects or simple inertia in the spread of HIV/AIDS. The baseline values of economic development, education, health spending, and percent Muslim

**Table 2:** OLS Test of Determinants of Change in HIV/AIDS Prevalence, 2000–2005

Independent Variable	Changes in AIDS Prevalence 2000–2005			
	Model 1	Model 2	Model 3	Model 4
HIV Prevalence 2000	0.791*** (0.084)	0.863*** (0.146)	0.683*** (0.095)	0.728*** (0.181)
Gender Index 2000	-4.818 (13.327)	-21.420 (28.295)	-17.955 (13.187)	-46.961 (30.121)
Change in Gender Index 2000–2005	–	–	-36.810## (13.313)	-27.589# (15.684)
Economic Development 2000	0.000 (0.000)	0.001 (0.001)	0.000 * (0.000)	0.001* (0.001)
Education Index 2000	5.703 (7.797)	10.798 (14.231)	8.825 (7.547)	16.780 (15.043)
Per Capita Health Spending 2000	0.366* (0.183)	0.381 (0.284)	0.311 (0.192)	0.160 (0.223)
Percent Muslim	–	0.015 (0.032)	–	-0.003 (0.032)
Constant	-4.123	-0.666	0.974	9.126
R-Sq.	0.868	0.868	0.901	0.905
N	34	26	31	23

# =  $p < 0.10$ ; ## =  $p < 0.05$ , one-tailed test. \* =  $p < 0.10$ ; \*\*\* =  $p < 0.01$ , two-tailed test; values between brackets are standard errors.

were also included in the models.<sup>10</sup> To control for ceiling or floor effects for gender equity, we include in two of the models (3 and 4) both the baseline 2000 and change from 2000 to 2005 values of the GDI while excluding the latter in Models 1 and 2. Finally, Models 1 and 3 again exclude percent Muslim in order to assess the sensitivity of the estimates for the gender equity to collinearity.

As might be expected, the positive and significant estimate of the 2000 value of HIV/AIDS prevalence indicates that there is considerable inertia in its spread. Countries with the highest levels of AIDS in 2000 experienced the fastest growth rates from 2000 to 2005. This inertia is so powerful that the effects of the control variables are greatly diminished in the change score models in Table 2; only per-capita health spending in Model 1 and economic development in Models 3 and 4 generate significant estimates at even modest criterion levels. Turning to the critical gender equity variables, it seems that the baseline level of gender equity in 2000 also has little independent impact on change in AIDS prevalence; while negative as expected, the

10. Again, change scores for these variables were also examined with few discernible effects. The estimates in Table 2 seem quite robust in the face of decisions to include or exclude these additional variables in the estimating models or to exclude outlying cases.

estimated values for GDI in Models 1 and 2 are smaller than their standard errors. Again, the effect of this variable seems to be largely captured through the inclusion in the models of the baseline 2000 values of the dependent variable. But as seen in Models 3 and 4, inclusion of both the 2000 level of GDI and its changes in value from 2000 to 2005 suggests that gender equity does indeed matter. That is, the estimates for GDI in both Models 3 and 4 are of considerably greater magnitude than those observed for Models 1 and 2. While again not surprising given the considerable inertia in AIDS infection found for all the control variables, neither 2000 GDI estimate in Models 3 and 4 is significant. Still, both are now considerably greater in magnitude than their standard errors. More importantly, and unlike the control variables, change in gender equity seems to matter. Both estimates of change in GDI from 2000 to 2005 in Models 3 and 4 are negative and discernibly different from zero.

## 8.5 CONCLUSIONS

We have found strong support for the expectation that gender equity influences HIV/AIDS-prevalence. Critically important in terms of public policy, it matters both in terms of level (Table 1) and change in AIDS prevalence (Table 2). That is, the results in Table 2 suggest that public policy efforts to improve levels of gender equity can have a marked impact on the spread of HIV/AIDS. Indeed, these effects suggest that this impact is rather large and impressive when compared to very weak effects found for comparable changes in levels of economic development, education, and health-care spending. And levels of gender equity are not constants even over the five-year timeframe we have examined. As noted earlier, while the static values of GDI across all sub-Saharan African countries ranged across 0.51 points in 2003, changes in these values within countries ranged across a full 0.27 points between 2000 and 2005. Thus, considerable change in gender equity is possible. As a consequence of public policy, then, efforts to improve gender equity might well influence the rate of change in HIV/AIDS prevalence.

Our finding that public policy efforts to improve gender equity can impact HIV-prevalence does, in itself, not justify the reallocation of resources. First, we fully admit that the composite GDI is a crude index that does not adequately reflect the specific ways in which gender equity might matter in specific places at specific times. We do not yet know how specific cultural practices and/or the precise nature of women's access to the levers of public policy influence exposure to and treatment of AIDS. In research design terms, these are issues of construct validity – precisely determining the specific elements of a general cause that influence an observed outcome. Second, once these issues of construct validity are addressed and policies

to improve gender equity are identified, it is not said they provide value for money, i.e., are cost-effective. Further attention to both these issues are the necessary next steps in our analysis as we seek to develop sound policy advice for African nations as they struggle with the manifest threats posed by the HIV/AIDS pandemic.

# Chapter 9

Discussion





## 9.1 INTRODUCTION

The main purpose of this thesis is to contribute to the understanding of the role and importance of affordability in relation to choices in health care and to its measurement. This will be done according to the research questions presented in the introduction:

1. **How can the affordability of health care services be measured in LMICs?**
2. **How can the concept of affordability inform choices regarding the benefit package of a mandatory health insurance system?**
3. **How can choices regarding the allocation of scarce resources be informed?**

After that, we will highlight some limitations and policy implications of our research and identify future research questions.

## 9.2 MAIN FINDINGS

### **PART I – Affordability at the micro level in low- and middle-income countries: the example of medicine affordability.**

The first part of this dissertation concerned the question how affordability of health care services can be measured in low- and middle-income countries (LMICs). We addressed this question focusing on medicines, as in LMICs medicines are mostly paid for out-of-pocket and constitute a major part of total health care expenditures. The World Health Organization and Health Action International express medicine affordability in the number of day's wages the Lowest Paid Government Worker (LPGW) needs to procure a course of treatment (Cameron et al., 2009b). The simplicity of this concept ensures its ease of calculation and intelligibility; people within a country can easily position themselves relative to the LPGW of that country. However, the metric may misrepresent affordability when many people earn more or less than the LPGW. Furthermore, it hampers cross-country comparison of medicine affordability as the LPGW-wage differs both in absolute and in relative terms between countries.

In chapters 2 and 3 we set out to explore and apply alternative applications of methods that address some of the limitations of the LPGW-concept. In **chapter 2** we explored two alternative applications of methods that can be and have been used to estimate medicine affordability: the catastrophic payment method and the impoverishment method. Within the catastrophic payment method a medicine is deemed unaffordable when its cost exceeds a certain proportion of the available income. The impoverishment method looks at the absolute level of available resources before and after procurement of a medicine. When due to the procurement of a medicine someone is pushed below a poverty line, the medicine is deemed unaffordable. The



use of these methods is commonly dependent on the availability of detailed household survey data which in LMICs often is not readily available. We showed that these methods can also be applied using aggregated data, which yielded quite favorable results. Of course, the usefulness of the proposed application of these methods with aggregated data depends largely on their validity. In that context, we highlighted that in Indonesia and India the World Development Indicators' household final consumption expenditure estimates are substantially higher than the income data collected in household surveys (Ravallion, 2003). As a result, the use of macro methods leads to underestimation of impoverishment assuming that micro approaches are more valid. In **chapter 2**, the main critique on the LPGW approach -i.e. that it may overestimate affordability- was confirmed, as in many countries a substantial proportion of the population earns less than the LPGW. In **chapter 3**, we compared the affordability of four medicines across sixteen countries with the impoverishment method based on macro-data. The results in this study illustrated that a substantial proportion of the population would be pushed into poverty as a result of medicine procurement, implying that in many LMICs the affordability of treatments is low and indeed lower than often reported (Cameron et al., 2009b; Niëns et al., 2010). We also found that the lowest priced generic medicines in general were substantially more affordable than originator brand products. Hence, increasing the use of quality-assured generics could reduce the impoverishing effect of medicines.

**Chapter 4** went deeper into the issue of an appropriate threshold to be used in defining and operationalizing the impoverishment and catastrophic payment methods. Such a choice obviously influences the affordability outcomes and cannot be unambiguously made. We showed the impact of the methods chosen to measure affordability, as well as the thresholds chosen within those methods, to be significant on final outcomes and argued that it may be worthwhile to create a (preliminary) standard for calculating affordability to increase comparability between studies. We suggested using both the impoverishment and catastrophic payment methods. Moreover, applying a (standard) range of thresholds would be a logical choice, given the current variation.

## **PART II – Affordability at the macro level in a developed country: delineating entitlements in systems of (social) health insurance.**

In the second part of this dissertation the central question focused on how the concept of affordability can inform choices regarding the benefit package of a mandatory health insurance system. We took the Netherlands as an example because, as in many high-income countries, the scope of its (social) health care insurance system is critically examined. The Dutch Health Care Insurance Board (CVZ) is responsible for advising the Ministry of Health on what should be included in the basic benefit

package of its mandatory health care insurance scheme. CVZ applies a ‘package management’ framework that consists of four criteria, i.e., *necessity*, *effectiveness*, *efficiency* and *feasibility*. The level of operationalization of these criteria differs in practice, however. Whereas *effectiveness* and *efficiency* are operationalized through the concepts of evidence-based medicine and cost-effectiveness, the operationalization of the *necessity* and *feasibility* criteria remains less clear. This is worrisome, since in Dutch public policy, the argument that interventions for which patients should be able to bear the costs themselves should not be part of the benefit package, appears to become more prominent. Therefore, **chapter 5** took forward the operationalization of the *necessity* criterion. Encompassing the elements of disease burden and ‘necessity of insurance’ (NoI), the *necessity* criterion serves to inquire if *the disease or required health care warrants a claim on solidarity given the cultural context*. More specifically, we focused on the NoI-element which concerns the question *whether it is socially necessary or appropriate to insure an intervention*. We showed the lack of an instrument to operationalize the NoI-element frustrated its application in CVZ’s decision making process and developed a checklist that should facilitate and standardize the inclusion of the NoI-element in the decision making process. Consisting of eight questions grouped under the themes of *health insurance as an instrument* and *financial accessibility*, the checklist improves the process of decision-making by making the arguments related to the NoI-element more transparent, consistent and comprehensive, thereby limiting arbitrariness. As a result, the decisions can be better explained and, ideally, will become more predictable.

### **PART III – Health economics at the macro level in low- and middle-income countries: choices in breast cancer and HIV/AIDS.**

In the first two parts of this dissertation we saw that in countries with both high and low levels of resources, issues of affordability are indeed important. The third and final part continued with studies that showed how health economics can help policymakers in making choices given scarcity of resources. As the first two parts of this dissertation made clear, policy makers in both high-income and LMICs face questions about how to keep health care affordable on the individual and societal levels. When policy makers make decisions at a societal level, good governance requires the process of reaching these decisions to be transparent, consistent and comprehensive (Daniels & Sabin, 1997; Daniels, 1999). The final three chapters in this dissertation used health economic techniques to inform those decisions. In **chapter 6** we studied the cost-effectiveness of various policy options in breast cancer care in Costa Rica and Mexico. In this chapter our results showed that both countries could benefit from scaling up their national breast cancer programs. Ideally the proportion of patients presenting themselves at earlier stages for treatment should

increase. As the yearly costs of mammography screening programs are very high, for both countries a mass-media campaign or a program of clinical breast examination screening might be interesting options for early detection and improvement of their respective breast cancer care programs. In **chapter 7**, we studied whether higher socio-economic status (SES) groups in Ghana had better health outcomes in breast cancer care. We found that even though in higher SES-groups more patients were diagnosed in earlier stages than in lower SES-groups, this difference was not statistically significant, which may be attributable to a small sample size. In **chapter 8**, we analyzed the relationship between different variables of the United Nations' Human Development Indicators and the change in HIV-prevalence in sub-Saharan Africa. In all our results, the Gender Development Index variable was found to have a highly significant, negative relationship with HIV-prevalence. Although causality has not been proven, this information may be useful for policymakers in that it suggests that developing policies to address gender inequality may have a significant impact on HIV-prevalence.

### 9.3 LIMITATIONS AND POLICY IMPLICATIONS

From the onset of this thesis, it was clear that affordability is a highly relevant yet inherently vague concept (Bradley, 2008). Only in a world with limitless resources affordability would not be an issue. This dissertation has shown that issues of affordability in health care are present in both low- and middle-income as well as in high-income countries, both at the patient and at the societal level. The main purpose of this dissertation was to increase the understanding of the affordability concept in health care. In considering the implications of our findings, it is important to address the limitations of our studies and to formulate future research questions.

A first limitation of this thesis relates to the research questions posed. For example, in chapters 2 and 3 we looked at the affordability of medicines. However, in estimating the affordability of health care, arguably, it is better to not consider a single category only. Indeed, studying the affordability of single medicines ignores the fact that health care treatments often encompass multiple medicines and physician or hospital services. The latter are often also paid for out-of-pocket in LMICs. Future research thus could focus on devising a standard regarding which costs to include and how to include them. Also, the question about how to calculate the affordability of medicines for acute conditions is not answered yet. Because these medicines are often used during short periods of time, patients can more easily resort to coping mechanisms like using their savings, borrowing or selling of assets.

Second, although the concepts of impoverishment and catastrophic payment are well accepted in the context of LMICs (Cameron et al., 2009a), in high-income countries their use can be more problematic. As we acknowledged in chapter 2, the application of the impoverishment and catastrophic expenditure methods depends to a large extent on a country's economic situation. In The Netherlands the trend is to exclude low-cost, affordable care from the basic benefits package (e.g. medical devices). One might use the aforementioned methods in setting limits to the costs of individual treatments, below which they can be left out of the package.<sup>1</sup> However, numerous problems arise in setting such a limit. First, it is unclear how this limit interferes with the general deductible in the Dutch health care system. Second, it is unclear how to deal with accumulating costs when more than one low-cost item is used, separately perhaps affordable, but jointly unaffordable. Third, in the Netherlands excluding interventions solely on the basis of affordability is uncommon, and more aspects are considered in the decision. In the Netherlands, the CVZ's package management process incorporates both efficiency and feasibility (which, among others, looks at the budget impact) criteria. Therefore, implementing additional co-payments, next to a mandatory deductible, for treatments that already passed CVZ's package management criteria (and thus efficiency requirements) leads to an interesting situation. The mandatory yearly deductible is much discussed in the Netherlands. First set at €150 when implemented in 2008 (van de Ven & Schut, 2008) it has increased to €220 in 2012 (Schut et al., 2013) and €350 in 2013 (van Ginneken et al., 2013). In chapter 5 we highlighted CVZ's Necessity of Insurance element, which encompasses the deliberations of the 1991 Dunning committee grouped under its 'own account and responsibility' criterion. It includes the argument that the costs of an intervention should play a role in decisions regarding their in-/exclusion into the basic benefit package. Given the broad range of considerations, of which affordability is just one, a fixed monetary threshold for affordability was not set. One may even question whether it is possible to set a clear and single threshold for affordability, since in a final decision to reimburse a specific health care technology many other factors may play a (more important) role.

Third, in different economic circumstances different thresholds play a role. Because in LMICs out-of-pocket payments make up a large portion of total health care expenditure, the required poverty line and proportion of income thresholds used when applying the impoverishment and catastrophic payment methods significantly influence what we deem affordable for an *individual*. Chapters 2, 3 and 4 all con-

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1. Using the catastrophic payment principle, taking 2.5% as the maximum proportion of income to be spent and the lowest level of Dutch social security payments ('Bijstand'), which is about €12,000 per year, one could derive a threshold of €300.

cerned the threshold from an individual perspective. When doing cost-effectiveness analysis in countries with national (social) health insurance systems like Costa Rica and Mexico, the cost-per-DALY averted threshold captures what is deemed good value for money for a *country*, which is related to what these countries can afford to pay for health care. Hence, in chapter 6 the threshold was used to identify the most efficient health care programs, which in a (social) health insurance system are then paid for publicly. However, the discussion about what the value or willingness to pay for a QALY gained or DALY averted is still ongoing (Culyer et al., 2007; McCabe et al., 2008; Bobinac et al., 2010; Shiroiwa et al., 2010). Furthermore, policymakers in Costa Rica and Mexico expressed the opinion that, although the efficiency of a treatment as measured in a cost-per-QALY/DALY is important, for them the budget impact was just as important. So whereas the cost-per-QALY/DALY threshold expresses, theoretically, what a country is willing to pay (given what they can afford), other considerations, including budget impact, may play an important role as well.

Fourth, in the cost-effectiveness analysis of breast cancer care in Costa Rica and Mexico in chapter 6 we had to rely on assumptions regarding the effectiveness of several interventions that involved either screening or raising awareness. This requires the results of several modeled scenarios to be interpreted with caution. However, sensitivity analyses showed our conclusions to be robust. Ideally, simultaneously to implementing a clinical breast examination screening program or a mass awareness raising program studies measuring the effect of these programs are implemented.

Fifth, in studying the equity of treatment outcomes in Ghanaian breast cancer care, the fact that in chapter 7 we did not find a statistically significant relationship between socio-economic status and the number of DALYs averted might be due to the small sample size. It was unfortunate that the available budget did not allow us to include the patient population from Ghana's second academic hospital (Korle Bu, Accra). Possibly this would have led to more robust results.

The main limitation of chapter 8 concerns the fact that the Gender Development Index is composite in nature. Although it expresses the differences between sexes on three dimensions (1 - life expectancy at birth; 2 - the adult literacy rate and the combined primary, secondary, and tertiary gross enrollment ratio in schools and 3 - the estimated income earned) the index does not provide information on how gender differences influence women's exposure to and treatment of HIV/AIDS. Policy makers would benefit from studies that help explain these issues of construct validity to improve policy advice for African nations struggling with the HIV/AIDS-epidemic. Of course, scarcity of resources requires to also study the efficiency of these policy options to further inform policymakers.

## 9.4 FUTURE RESEARCH

This thesis provides more insight in the issue of affordability in health care. Nonetheless, the above introduced limitations are real and warrant further research.

First, comparing affordability of health care across borders is difficult due to differences in prices, income and health care financing. In those countries where OOP-payments account for the majority of health care expenditures, to improve the comparability of affordability, the costs of a 'basic basket of health care interventions' should be studied using purchasing power parities.

Second, although the developed checklist structures the debate concerning the necessity of insurance element of the necessity criterion in the Netherlands, guidelines for how to answer these questions are not developed yet. Developing these would be a next logical step in the process of increasing transparency, consistency and comprehensiveness in these decisions.

Third, while cost-effectiveness studies provide useful information for policy makers, priority setting decisions are complex as many other considerations play a role (Baltussen & Niessen, 2006). Future research could focus on using multi-criteria-decision-analysis to help policy makers in both Costa Rica and Mexico, to inform their decisions in breast cancer.

Although affordability remains a vague concept, the problems surrounding it are real. This holds for people not being able to pay for essential health care (e.g. medicines), governments struggling with keeping their national (social) health insurance systems affordable and researchers attempting to meaningfully operationalize and measure affordability. Because the impact of policy decisions on the affordability of health care can be large as can be the health impact of such decisions, increasing the understanding of affordability and providing policy makers and politicians with better information to inform their policy decisions is important. Inefficient health care and increasing levels of inequity are things we certainly cannot afford.



## References

- Adjuvant Online. Adjuvant! Online. Decision making tools for health care professionals. 2010; Available at: [www.adjuvantonline.com](http://www.adjuvantonline.com). Accessed January 5, 2011.
- Africa news. Rich Nigerians Will Always Travel Abroad For Medical Treatment. 2010; Available at: [http://www.africanews.com/site/list\\_message/29673](http://www.africanews.com/site/list_message/29673). Accessed June 6th, 2011.
- Agarwal G, Ramakant P, Forgach ER, Rendon JC, Chaparro JM, Basurto CS, et al. Breast cancer care in developing countries. *World J Surg* 2009 Oct;33(10):2069-2076.
- Akeroyd AV. Coercion, Constraints and 'Cultural Entrapments': A Further Look at Gendered and Occupational Factors Pertinent to the Transmission of HIV in Africa.. In: Kalipeni E, Craddock S, Opong JR, Gosh J, editors. *HIV and AIDS in Africa: beyond epidemiology* Oxford, UK: Blackwell Publishing; 2004.
- Althuis MD, Dozier JM, Anderson WF, Devesa SS, Brinton LA. Global trends in breast cancer incidence and mortality 1973-1997. *Int J Epidemiol* 2005 -03;34(2):405-412.
- Anderson BO, Carlson RW. Guidelines for improving breast health care in limited resource countries: the Breast Health Global Initiative. *J Natl Compr Canc Netw* 2007;5(3):349--56.
- Anderson BO. Breast Cancer in Limited-Resource Countries: Health Care Systems and Public Policy. *Breast J* 2006;12(1):S54.
- Anderson BO, Cazap E, El Saghir NS, Yip CH, Khaled HM, Otero IV, et al. Optimisation of breast cancer management in low-resource and middle-resource countries: executive summary of the Breast Health Global Initiative consensus, 2010. *Lancet Oncol* 2011 Apr;12(4):387-398.
- Anderson BO, Shyyan R, Eniu A, Smith RA, Yip CH, Bese NS, et al. Breast cancer in limited-resource countries: an overview of the Breast Health Global Initiative 2005 guidelines. *Breast J* 2006 Jan-Feb;12 Suppl 1:S3-15.
- Asante F, Aikens M. Does the NHIS cover the poor? *Age (Omaha)* 2007;26:27.
- Backman G, Hunt P, Khosla R, Jaramillo-Strouss C, Fikre BM, Rumble C, et al. Health systems and the right to health: an assessment of 194 countries. *Lancet* 2008 Dec 13;372(9655):2047-2085.
- Bailey RC. Male circumcision and HIV prevention: current knowledge and future research directions. *The Lancet infectious diseases* 2001 -11;1(4):223-231.
- Baltussen R, Niessen L. Priority setting of health interventions: the need for multi-criteria decision analysis. *Cost Eff Resour Alloc* 2006 Aug 21;4:14.
- Barros PP, Machado SR, Simoes Jde A. Portugal. Health system review. *Health Syst Transit* 2011;13(4):1-156.
- Baylies C, Burja J editors. *Discourses of Power and Empowerment in the Fight Against HIV/AIDS in Africa*. London: Taylor and Francis; 1995.
- Blackstock AW, Herndon JE, 2nd, Paskett ED, Miller AA, Lathan C, Niell HB, et al. Similar outcomes between African American and non-African American patients with extensive-stage small-cell lung carcinoma: report from the Cancer and Leukemia Group B. *J Clin Oncol* 2006 Jan 20;24(3):407-412.
- Bland KI, Menck HR, Scott-Conner CEH, Morrow M, Winchester DJ, Winchester DP. The National Cancer Data Base 10-year survey of breast carcinoma treatment at hospitals in the United States. *Cancer* 1998;83(6):1262-1273.



- Bloom HJG, Richardson WW, Harries EJ. Natural History of Untreated Breast Cancer (1805-1933). *BMJ. British medical journal (Clinical research ed.)* 1962 -07;2(5299):213-221.
- Bobinac A, Van Exel NJ, Rutten FF, Brouwer WB. Willingness to pay for a quality-adjusted life-year: the individual perspective. *Value Health* 2010 Dec;13(8):1046-1055.
- Bobo JK, Lee NC, Thames SF. Findings From 752 081 Clinical Breast Examinations Reported to a National Screening Program From 1995 Through 1998. *JNCI : Journal of the National Cancer Institute* 2000 -06;92(12):971-976.
- Boonen LHHM, van der Geest SA, Schut FT, Varkevisser M. Pharmaceutical Markets and Insurance Worldwide Pharmaceutical policy in the Netherlands: From price regulation towards managed competition. *Advances in health economics and health services research*; 2010. p. 53-76.
- Bradley R. Comment - defining health insurance affordability: unobserved heterogeneity matters. *J Health Econ* 2008 Jul;27(4):1129-1140.
- Braveman P, Gruskin S. Defining equity in health. *J Epidemiol Community Health* 2003 Apr;57(4):254-258.
- Brown LR. Economic Growth Rates in Africa: The Potential Impact of HIV/AIDS. In: Kalipeni E, Craddock S, Oponng JR, Gosh J, editors. *HIV&AIDS in Africa—Beyond Epidemiology* Oxford, UK: Blackwell Publishing.; 2004.
- Bruce S, Grana J. Ability to Pay and the Decision to Medicate. *Med Care* 1998 Feb.;36(2):202-211.
- Bundorf MK, Pauly MV. Is health insurance affordable for the uninsured? *J Health Econ* 2006 Jul;25(4):650-673.
- Business Guide. Accra, Ashanti Lead Income Growth. 2011; Available at: <http://www.business-guideghana.com/?p=3683>. Accessed July 26th, 2011.
- Cameron A, Ewen M, Auton M, Laing R. Better measures of affordability required – Authors' reply. *The Lancet (British edition)* 2009a -03;373(9669):1081;-1082;.
- Cameron A, Ewen M, Ross-Degnan D, Ball D, Laing R. Medicine prices, availability, and affordability in 36 developing and middle-income countries: a secondary analysis. *Lancet* 2009b Jan 17;373(9659):240-249.
- Campbell JD, Ramsey SD. The costs of treating breast cancer in the US: a synthesis of published evidence. *Pharmacoeconomics* 2009;27(3):199-209.
- Carruthers R, Dick M, Saurkar A. Affordability of Public Transport in Developing Countries. 2005;Transport Papers TP-3.
- Chandra A, Skinner JS. Technology growth and expenditure growth in health care. *Journal of Economic Literature* 2012;50(3):645-680.
- Charry LC, Carrasquilla G, Roca S. Equity regarding early breast cancer screening according to health insurance status in Colombia. *Rev Salud Publica (Bogota)* 2008 Aug-Oct;10(4):571-582.
- Chen S, Ravallion M. The developing world is poorer than we thought, but no less successful in the fight against poverty. 2008.
- College voor Zorgverzekeringen. Functiegerichte omschrijving hulpmiddelen voor het bewegingssysteem. 2012.
- College voor Zorgverzekeringen. Incontinentie absorptiemateriaal: noodzakelijk te verzekeren zorg? 2011a.
- College voor Zorgverzekeringen. Taking care of health care - Information about the Health Care Insurance Board. 2011b;2013(January, 16).
- College voor Zorgverzekeringen. Pakketbeheer in de praktijk II. 2009a.

- College voor Zorgverzekeringen. Stoppen-met-rokenprogramma: te verzekeren zorg! 2009b.
- College voor Zorgverzekeringen. Beoordelingskader hulpmiddelenzorg. 2008a.
- College voor Zorgverzekeringen. Hulpmiddelenzorg 2008 - (Deelrapport van het pakketadvies 2008). 2008b.
- College voor Zorgverzekeringen. Pakketbeheer in de praktijk. 2006.
- College voor Zorgverzekeringen. Breedte geneesmiddelenpakket. 2001;01/54.
- Collingridge D. Delivering consensus from the Asian Oncology Summit 2009. *Lancet Oncol* 2009 Nov;10(11):1029-1030.
- Comisión Nacional de Protección Social en Salud. Casos Registrados y Validados de Cáncer de Mama en el SIGGC 2010. 2011.
- Commissie Criteria Geneesmiddelenkeuze (chair: van Winzum). Verdeling door verdunning. Kiezen en delen: de geneesmiddelenvoorziening in Nederland. 1994.
- Connell RW. *Gender and Power: Society, the Person and Sexual Policies*. Stanford, CA: Stanford University Press.; 1987.
- Connell J. Medical tourism: Sea, sun, sand and... surgery. *Tourism management* 2006;27(6):1093.
- Consejo Nacional de Población. *Proyecciones Poblacionales 2005-2050*, México. 2011; Available at: <http://www.conapo.gob.mx>. Accessed October 2011, 2011.
- Costa Font J, Sato A. Health systems futures: The challenges of technology, prevention and insurance. *Futures* 2012 9;44(7):696-703.
- Culyer A, McCabe C, Briggs A, Claxton K, Buxton M, Akehurst R, et al. Searching for a threshold, not setting one: the role of the National Institute for Health and Clinical Excellence. *J Health Serv Res Policy* 2007 Jan;12(1):56-58.
- Daniels N. Decisions about access to health care and accountability for reasonableness. *J Urban Health* 1999 Jun;76(2):176-191.
- Daniels N, Sabin J. Limits to health care: fair procedures, democratic deliberation, and the legitimacy problem for insurers. *Philos Public Aff* 1997 Fall;26(4):303-350.
- Devi BCR. Reducing by half the percentage of late-stage presentation for breast and cervix cancer over 4 years: a pilot study of clinical downstaging in Sarawak, Malaysia. *Annals of oncology* 2007;18(7):1172-1176.
- Dignam JJ, Colangelo I, Tian W, Jones J, Smith R, Wickerham LD, et al. Outcomes Among African-Americans and Caucasians in Colon Cancer Adjuvant Therapy Trials: Findings From the National Surgical Adjuvant Breast and Bowel Project. *JNCI : Journal of the National Cancer Institute* 1999 -11;91(22):1933-1940.
- Dolbear CN. *Housing Grants for the Very Poor*. Philadelphia: Philadelphia Housing Association; 1966.
- Dror DM, Preker AS, Jakab M. The role of communities in combating social exclusion. In: Dror DM, Preker AS, editors. *Social Reinsurance - A New Approach to Sustainable Community Health Financing* Washington DC; Geneva: The World Bank Group and the International Labour Office; 2002.
- Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. New York: Oxford University Press; 2005.
- Duffy SW, Gabe R. What should the detection rates of cancers be in breast screening programmes? *Br J Cancer* 2005 -01;92(3):597.
- Dunning A.J. *Kiezen en delen - Advies in Hoofdzaken Van De Commissie Keuzen in De Zorg*. 1991.

- Dylst P, Vulto A, Simoens S. The impact of reference-pricing systems in Europe: a literature review and case studies. *Expert Rev Pharmacoeconomics Outcomes Res* 2011 -12;11(6):729-737.
- Errico KM, Rowden D. Experiences of Breast Cancer Survivor-Advocates and Advocates in Countries with Limited Resources: A Shared Journey in Breast Cancer Advocacy. *Breast J* 2006;12(s1):S111-S116.
- Evans DB, Tan-Torres Edejer T, adam T, Lim SS. Methods to assess the costs and health effects of interventions for improving health in developing countries. *BMJ. British medical journal (Clinical research ed.)* 2005 -11;331(7525):1137-1140.
- Feenstra TL, Hamberg-van Reenen HH, Hoogenveen RT, Rutten-van Mólken MPMH. Cost-Effectiveness of Face-to-Face Smoking Cessation Interventions: A Dynamic Modeling Study. *Value in health* 2005 -05;8(3):178-190.
- Ferlay J, Bray F, Pisani P, Parkin DM. *GLOBOCAN 2002: cancer incidence, mortality and prevalence worldwide [CD-ROM]*. 2004.
- Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: *GLOBOCAN 2008*. *Int J Cancer* 2010 Dec 15;127(12):2893-2917.
- Fernández I. Diagnóstico Situacional para la Universalización de la Mastografía de Detección. Grupo Interinstitucional de Universalización de la Mastografía de Detección, June 8th, 2012;document presented to the Mexican Ministry of Health.
- Flannery J, Sullivan P. Female breast cancer in Connecticut—incidence, mortality, survival—1935–1975. *Connecticut Health Bulletin* 1978;92(1):4–9.
- Fleming ID, Cooper JS, Murphy GP, Sullivan BO, Sobin LH, Yarbro JW, et al. *American Joint Committee on Cancer: AJCC Cancer Staging Manual*. 5th ed. Philadelphia, PA: Lippincott-Raven; 1997.
- Flores G, Krishnakumar J, O'Donnell O, Van Doorslaer E. Coping with health-care costs: implications for the measurement of catastrophic expenditures and poverty. *Health Econ* 2008 Dec;17(12):1393-1412.
- Flores-Luna L, Salazar-Martínez E, Duarte-Torres EM, Torres-Mejía G, Alonso-Ruiz P, Lazcano-Ponce E. Factores pronósticos relacionados con la supervivencia del cáncer de mama. *Salud pública de México* 2008;50(2):119.
- Folland S, Goodman AG, Stano M. *The Economics of Health and Health Care*. 4th ed. Upper Saddle River, NJ 07458: Pearson Prentice Hall; 2004.
- Ford N, Wilson D, Costa Chaves G, Lotrowska M, Kijtiwatchakul K. Sustaining access to anti-retroviral therapy in the less-developed world: lessons from Brazil and Thailand. *AIDS (London)* 2007;21(suppl 4):S21-S29.
- Franco-Marina F, Lazcano-Ponce E, Lopez-Carillo L. Breast cancer mortality in Mexico: an age-period-cohort analysis. *Salud pública de México* 2009;51(suplemento 2):S157.
- Franken M, le Polain M, Cleemput I, Koopmanschap M. Similarities and differences between five European drug reimbursement systems. *Int J Technol Assess Health Care* 2012 Oct;28(4):349-357.
- Frankhauser S, Tepic S. Can poor consumers pay for energy and water? An affordability analysis for transition countries. 2005;Working paper no. 92.
- Fuchs VR. Economics, values, and health care reform. *Am Econ Rev* 1996 Mar;86(1):1-24.
- Fundación Cim\*ab. 2011; Available at: <http://www.cimab.org/index.html>. Accessed October 19, 2011.
- Fundacion Nacional de Solidaridad Contra el Cancer de Mama. 2011; Available at: <http://www.fundeso.or.cr/>. Accessed October 19, 2011.

- Ginneken van E, Swartz K, Van der Wees P. Health Insurance Exchanges In Switzerland And The Netherlands Offer Five Key Lessons For The Operations Of US Exchanges. *Health Affairs* 2013;32(4):744-752.
- Ginsberg GM, Lauer JA, Zelle S, Baeten S, Baltussen R. Cost effectiveness of strategies to combat breast, cervical, and colorectal cancer in sub-Saharan Africa and South East Asia: mathematical modeling study. *BMJ* 2012 Mar 2;344:e614.
- González-Robledo LM, González-Robledo MC, Nigenda G, López-Carrillo L. Acciones gubernamentales para la detección temprana del cáncer de mama en América Latina. Retos a Futuro. *Salud pública de México* 2010;52(6):533-10.
- Government of India. Planning Commission. 2010; Available at: <http://planningcommission.nic.in/index.php>. Accessed August 12, 2011.
- Gray PB. HIV and Islam: is HIV prevalence lower among Muslims? *Social Science and Medicine* 2004 -05;58(9) :1751-1756.
- Greene FL, Compton CC, Fritz AG, Al E. *AJCC Cancer staging atlas*. New York, NY: Springer Inc; 2006.
- Groot MT, Baltussen R, Uyl-de Groot CA, Anderson BO, Hortobagyi GN. Costs and health effects of breast cancer interventions in epidemiologically different regions of Africa, North America, and Asia. *Breast J* 2006 Jan-Feb;12 Suppl 1:S81-90.
- Halperin DT, Potts M, Kirby D, Swidler A, Marseille E, Klausner JD, et al. Reassessing HIV prevention. *Science* 2008;320(5877):749.
- Ham C. Priority setting in health care: learning from international experience. *Health Policy* 1997 Oct;42(1):49-66.
- Hancock KE. 'Can Pay? Won't Pay?' or Economic Principles of 'Affordability'. *Urban studies* (Harlow) 1993;30(1):127-145.
- Harford JB, Otero IV, Anderson BO, Cazap E, Gradishar WJ, Gralow JR, et al. Problem solving for breast health care delivery in low and middle resource countries (LMCs): consensus statement from the Breast Health Global Initiative. *Breast J* 2011;20:S20eS29.
- Health Action International. *Medicine Prices*. 2012; Available at: <http://www.haiweb.org/medicineprices/>. Accessed July/1, 2013.
- Health Sector Advisory Office. Discussion paper: targeting the poor. Discussion of effectiveness, leakage, cost and acceptability. 2008 December 4.
- Helble M. The movement of patients across borders: challenges and opportunities for public health. *Bull World Health Organ* 2011;89:68.
- Herrick DM. Medical Tourism: Global Competition in Health Care. 2007;304.
- Hoogendoorn M, Feenstra TL, Hoogenveen RT, Rutten-van Mölken MPMH. Long-term effectiveness and cost-effectiveness of smoking cessation interventions with patients with COPD. *Thorax* 2010;65:711--718.
- Hortobagyi GN. Novel approaches to the management of bone metastases in patients with breast cancer. *Semin Oncol* 2002;29(3):134.
- Hulchanski JJD. The concept of housing affordability: Six contemporary uses of the housing expenditure-to-income ratio. *Housing studies* 1995;10(4):471-491.
- Hunt CW. Migrant Labor and Sexually Transmitted Disease: AIDS in Africa. *Journal of Health and Social Behavior* 1989;30(4):353--73.
- Hunter DJ. *Desperately Seeking Solutions, Rationing Health Care*. New York: Longman; 1997.
- Instituto Mexicano del Seguro Social, Unidad Análisis Económico. *modelo economico de micro-costeo de cancer de mama y cervix*. 2012.

- International Agency for Research on Cancer. GLOBOCAN 2008. 2012; Available at: <http://globocan.iarc.fr/>. Accessed October, 2011.
- International Agency for Research on Cancer Working Group on the Evaluation of Cancer-Preventive Strategies. Handbooks of Cancer Prevention, vol. 7, Breast Cancer Screening. Lyon, France: IARC Press; 2002.
- International Diabetes Federation. 2010; Available at: <http://archive.diabetesatlas.org>. Accessed February/16, 2010.
- Jatoi I, Anderson WF, Rao SR, Devesa SS. Breast cancer trends among black and white women in the United States. *J Clin Oncol* 2005 Nov 1;23(31):7836-7841.
- Jehu-Appiah C, Aryeetey G, Spaan E, de Hoop T, Agyepong I, Baltussen R. Equity aspects of the National Health Insurance Scheme in Ghana: Who is enrolling, who is not and why? *Soc Sci Med* 2011 Jan;72(2):157-165.
- Jehu-Appiah C, Aryeetey G, Spaan E, Agyepong I, Baltussen R. Efficiency, equity and feasibility of strategies to identify the poor: An application to premium exemptions under National Health Insurance in Ghana. *Health policy (Amsterdam)* 2010;95(2-3):166.
- Joseph Sheehan T, DeChello LM, Kulldorff M, Gregorio DI, Gershman S, Mrosczyk M. The geographic distribution of breast cancer incidence in Massachusetts 1988 to 1997, adjusted for covariates. *Int J Health Geogr* 2004 Aug 3;3(1):17.
- Kam de F. Gezondheidszorg en Openbare Financiën. In: Schut FT, F.F.H R, editors. *Economie van de gezondheidszorg*. 1e ed. Maarssen: Elsevier Gezondheidszorg; 2009.
- Kerr DJ, Midgley R. Can we treat cancer for a dollar a day? Guidelines for low-income countries. *N Engl J Med* 2010 Aug 26;363(9):801-803.
- Kesby M. Participatory Diagramming and the Ethical and Practical Challenges of Helping Africans Themselves to Move HIV Work 'Beyond Epidemiology'. In: Kalipeni E, Craddock S, Oppong JR, Gosh J, editors. *HIV&AIDS in Africa—Beyond Epidemiology* Oxford, UK: Blackwell; 2004.
- Khan SA, Stewart AK, Morrow M. Does aggressive local therapy improve survival in metastatic breast cancer? *Surgery* 2002 Oct;132(4):620-6; discussion 626-7.
- Knaul F, Arreola H, Méndez O, Miranda M. Preventing impoverishment, promoting equity and protecting households from financial crisis: universal health insurance through institutional reform in Mexico. 2006.
- Knaul FM, Arreola-Ornelas H, Velázquez E, Dorantes G, Méndez Ó, Ávila-Burgos L. El costo de la atención médica del cáncer mamario: el caso del Instituto Mexicano del Seguro Social. *Salud pública de México* 2009;51(suppl 2).
- Knaul FM, Frenk J. Health Insurance In Mexico: Achieving Universal Coverage Through Structural Reform. *Health affairs (Millwood, Va.)* 2005 -11;24(6):1467-1476.
- Knaul FM, Nigenda G, Lozano R, Areona-Ornelas H, Langer A, Frenk J. Breast cancer in Mexico: a pressing priority. *Reprod Health Matters* 2008;16(32):113.
- Kolasa K, Wasiak R. Health technology assessment in Poland and Scotland: comparison of process and decisions. *Int J Technol Assess Health Care* 2012 Jan;28(1):70-76.
- Komives K, Foster V, Halpern J, Wodon Q. Water, electricity, and the poor: Who benefits from utility subsidies? 2005.
- Kongsri S, Limwattananon S, Sirilak S, Prakongsai P, Tangcharoensathien V. Equity of access to and utilization of reproductive health services in Thailand: national Reproductive Health Survey data, 2006 and 2009. *Reprod Health Matters* 2011 May;19(37):86-97.

- Koning de HJ, van Ineveld BM, van Oortmarssen GJ, de Haes JCJM, Collette HJA, Hendriks JHCL, et al. Breast cancer screening and cost-effectiveness; Policy alternatives, quality of life considerations and the possible impact of uncertain factors. *International journal of cancer* 1991 -10;49(4):531-537.
- Kumar SK. Kerala, India: A Regional Community-Based Palliative Care Model. *J Pain Symptom Manage* 2007;33(5):623-627.
- Kutty NK. A new measure of housing affordability: Estimates and analytical results. *Housing policy debate* 2005;16(1):113-142.
- Lagarde E, Enel C, Seck K, Gueye-Ndiaye A, Piau JP, Pison G, et al. Religion and protective behaviours towards AIDS in rural Senegal. *AIDS* 2000 Sep 8;14(13):2027-2033.
- Lagarde M, Palmer N. The impact of user fees on access to health services in low- and middle-income countries. *Cochrane Database Syst Rev* 2011 Apr 13;(4)(4):CD009094.
- Lantz PPM. The Influence of Race, Ethnicity, and Individual Socioeconomic Factors on Breast Cancer Stage at Diagnosis. *American journal of public health (1971)* 2006;96(12):2173-2178.
- Lauer JA, Rohrich K, Wirth H, Charette C, Gribble S, Murray CJ. PopMod: a longitudinal population model with two interacting disease states. *Cost Eff Resour Alloc* 2003 Feb 26;1(1):6.
- Launois R, Reboul-Marty MJ, Henry B, Bonnetterre J. A cost-utility analysis of second line chemotherapy in metastatic breast cancer. *Pharmacoeconomics* 1996;10:504.
- le Polain M, Franken M, Koopmanschap M, Cleemput I. Drug reimbursement systems: international comparison and policy recommendations. *Health Services Research (HSR)* 2010;KCE Reports 147C.
- Leatherman S, Ferris TG, Berwick D, Omaswa F, Crisp N. The role of quality improvement in strengthening health systems in developing countries. *Int J Qual Health Care* 2010 Aug;22(4):237-243.
- Lee YC, Yang MC, Huang, Y.T. Liu, C.H., Chen SB. Impacts of Cost Containment Strategies on Pharmaceutical Expenditures of the National Health Insurance in Taiwan, 1996-2003. *Pharmacoeconomics* 2006;24(9):891.
- Lieberman EES. Ethnic Politics, Risk, and Policy-Making: A Cross-National Statistical Analysis of Government Responses to HIV/AIDS. *Comparative political studies* 2007 -09;40(12):1407-1432.
- Limwattananon S, Tangcharoensathienb V, Prakongsai P. Catastrophic and poverty impacts of health payments: results from national household surveys in Thailand. *Bull World Health Organ* 2007;85(8):600.
- Lipton, M., Ravallion, M. Poverty and Policy. In: Behrman, J., Srinivasan, T.N., editor. *Handbook of Development Economics* Amsterdam; 1994.
- Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *The Lancet (British edition)* 2006;367(9524):1747-1757.
- López-Ríos O, Lazcano-Ponce EC, Tovar-Guzmán V, Hernández-Avila M. La epidemia de cáncer de mama en México.¿ Consecuencia de la transición demográfica? *Salud pública de México* 1997;39(4).
- Lu C, Chin B, Lic G, Murray CJL. Limitations of methods for measuring out-of-pocket and catastrophic private health expenditures. *Bull World Health Organ* 2009;87(3):238.

- Luijn van JCF, Loenhout JWH, Riteko JA, Ripken T,. Toetsing van het geneesmiddelenpakket. Het 'Beslismodel extramurale farmaceutische hulp' van de Ziekenfondsraad. *Medisch Contact* 1995;50(45):1433--1437.
- Magrath I, Litvak J. Cancer in developing countries: opportunity and challenge. *J Natl Cancer Inst* 1993 Jun 2;85(11):862-874.
- Marmot M. *Status Syndrome—How Your Social Standing Directly Affects Your Health*. London: Bloomsbury; 2004.
- Martínez-Montañez OG, Uribe-Zúñiga P, Hernández-Ávila M. Políticas públicas para la detección del cáncer de mama en México. *Salud pública de México* 2009;51:s350-s360.
- Mbulaiteye SM, Ruberantwari A, Nakiyingi JS, Carpenter LM, Kamali A, Whitworth JA. Alcohol and HIV: a study among sexually active adults in rural southwest Uganda. *Int J Epidemiol* 2000 Oct;29(5):911-915.
- McCabe C, Claxton K, Culyer AJ. The NICE cost-effectiveness threshold: what it is and what that means. *Pharmacoeconomics* 2008;26(9):733-744.
- McDavid K, Tucker TC, Sloggett A, Coleman MP. Cancer survival in Kentucky and health insurance coverage. *Arch Intern Med* 2003 Oct 13;163(18):2135-2144.
- McFadden P. Sex, Sexuality and the Problems of AIDS in Africa. In: Meena R, editor. *Gender in Southern Africa: Conceptual and Theoretical Issues*. Harare: Sapes Books; 1992.
- McIntosh C. The Relationship Between Health Care Provision and AIDS Prevalence in Sub-Saharan Africa. Paper presented to the Working Group in African Political Economy (WGAPE) Berkeley, CA 2006.
- McIntyre D, Thiede M, Dahlgren G, Whitehead M. What are the economic consequences for households of illness and of paying for health care in low- and middle-income country contexts? *Soc Sci Med* 2006;62(4):858-865.
- Meltzer MI. Introduction to health economics for physicians. *The Lancet (British edition)* 2001 -09;358(9286):993-998.
- Meursing K. *A World of Silence: Living with HIV in Matabeleland, Zimbabwe*. Amsterdam: Royal Tropical Institute.; 1997.
- Mgalla Z, Wambura L, de Bruyn M. Gender and HIV/AIDS/STDs. In: Ng'weshemi J, Boerma T, Bennett J, Schapink D, editors. *Prevention and AIDS Care in Africa: A District Level Approach*. Amsterdam: KIT Press; 1997.
- Miller D, Livingstone V, Herbison GP. Interventions for relieving the pain and discomfort of screening mammography. 2008(1).
- Milne C. Telecoms demand: measures for improving demand in developing countries – a toolkit for action, Main Report (World Dialogue on Regulation). 2006.
- Ministerio de Salud. Mama Quirúrgica. In: Calvo Cháves Y, Vargas Chacón G, Tristán Trelles F, Rojas Montero F, Picado Iagos A, Rodríguez Jiménez L, et al, editors. *Normas y Procedimientos para el Tratamiento del Cáncer en Costa Rica* San José: Ministerio de Salud; 2009. p. 22.
- Ministerio de Salud. Incidencia y Mortalidad del Cáncer en Costa Rica - 1995 - 2005. 2007:1-63.
- Ministerio de Salud. Manual: "Guía de Atención integral para el Cáncer de Mama". *La Gaceta, diario oficial*, 2000 14 September;28851 - S:1-138.
- Ministry of Statistics and Program Implementation. Miro Data Archive. 2011; Available at: [http://mospi.nic.in/Mospi\\_New/site/home.aspx](http://mospi.nic.in/Mospi_New/site/home.aspx). Accessed June/8, 2011.
- Murakami Y, Blom A. Accessibility and Affordability of Tertiary Education in Brazil, Colombia, Mexico and Peru within a Global Context. 2008;Policy Research Working Paper 4517.

- Murray CJL, Lopez AD. The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability From Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020. *Global Burden of Disease and Injury 1996*.(vol. 1,).
- Newhouse JP. Medical care costs: how much welfare loss? *J Econ Perspect* 1992 Summer;6(3):3-21.
- Niëns LM, Brouwer WBF, Cameron A, Ewen M, Laing R. The affordability of medicines—a cross-national study. Rotterdam: Erasmus University 2009.
- Niëns LM, Brouwer WBF. Better measures of affordability required. *Lancet* 2009 Mar 28;373(9669):1081; author reply 1081-2.
- Niëns LM, Van de Poel E, Cameron A, Ewen M, Laing RO. Practical measurement of affordability: an application to medicines. Rotterdam: Institute of Health Policy and Management, Erasmus University, Working Paper W2009 02 2009.
- Niëns LM, Van de Poel E, Cameron A, Ewen M, Laing RO, Brouwer WBF. Practical measurement of affordability: an application to medicines. *Bull World Health Organ* 2012 -03;90(3):219-227.
- Niëns LM, Versteegh MM. Plafond voor eigen bijdragen in de zorg. 2011; Available at: <http://www.volkskrant.nl/vk/nl/3184/opinie/article/detail/2447257/2011/06/17/Plafond-voor-eigen-bijdragen-in-de-zorg.dhtml>. Accessed June, 17, 2011.
- Niëns LM, Cameron A, Van de Poel E, Ewen M, Brouwer WB, Laing R. Quantifying the impoverishing effects of purchasing medicines: a cross-country comparison of the affordability of medicines in the developing world. *PLoS Med* 2010 Aug 31;7(8):e1000333.
- Noell J, Biglan A, Berendt J, Ochs L, Metzler CW, Ary D, et al. Problematic Sexual Situations for Adolescents: Alcohol and Unsafe Sex. *American Journal of Health Behavior* 1993;17(6):40—49.
- Norum J. Breast cancer screening by mammography in Norway. Is it cost-effective? *Ann Oncol* 1999;10(2):197-203.
- Norum J, Risberg T, Olsen JA. A monoclonal antibody against HER-2 (Trastuzumab) for metastatic breast cancer: a model-based cost-effectiveness analysis. *Ann Oncol* 2005 Jun;16(6):909-914.
- Nyarko KM. Disease Control and Prevention Department, Ghana Health Service, Accra, Ghana. 2011.
- Nyman JA. The value of health insurance: the access motive. *J Health Econ* 1999;18(2):141.
- Oanda. Forex Trading and Exchange Rate Services. 2013; Available at: <http://www.oanda.com/>. Accessed May 3, 2013.
- O'Donnell O, Van Doorslaer E, Wagstaff A, Lindelow M. Analyzing Health Equity Using Household Survey Data – A Guide to Techniques and Their Implementation. Washington DC: The World Bank Group; 2008.
- Ohene-Yeboah M, Adjei E. Breast cancer in Kumasi, Ghana. *Ghana medical journal* 2012;46(1):8-13.
- Oppong JR, Agyei-Mensah S'. HIV/AIDS in West Africa: The Case of Senegal, Ghana, and Nigeria. In: Kalipeni E, Craddock S, Oppong JR, Gosh J, editors. *HIV&AIDS in Africa—Beyond Epidemiology* Oxford, UK: Blackwell Publishing.; 2004.
- Organization for Economic Co-operation and Development. *Health at a glance: Europe* 2012. 2012.
- Organization for Economic Co-operation and Development. *Health at a glance: Europe* 2010. 2010.



- Organization for Economic Co-operation and Development. Projecting OECD Health and Long Term Care Expenditures: What are the Main Drivers? Economic Department Working Paper 2006;477.
- Organization for Economic Co-operation and Development. Social issues in the provision and pricing of water service. 2003.
- Ortiz A. Supervivencia de las mujeres con cáncer de mama según desarrollo humano, Costa Rica 2000-2003. Tesis de Maestría en Salud Pública 2007.
- Orubuloye IO, Oguntimehin F, Sadiq T. Women's Role in Reproductive Health Decision Making and Vulnerability to STD and HIV/AIDS in Ekiti, Nigeria. *Health Transition Review* 1996;7(Suppl.):329–36.
- Pal SK, Mittal B. Fight against cancer in countries with limited resources: the post-genomic era scenario. *Asian Pac J Cancer Prev* 2004 Jul-Sep;5(3):328-333.
- Palacio-Mejía LS, Lazzano-Ponce E, Allen-Leigh B, Hernández-Ávila M. Diferencias regionales en la mortalidad por cáncer de mama y cérvix en México entre 1979 y 2006. *Salud pública de México* 2009;51:s208-s219.
- Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. *International journal of cancer* 1999;80(6):827-841.
- Parkin DM, Bray F, Ferlay J, Pisani P. *Global Cancer Statistics, 2002*. CA: a cancer journal for clinicians 2005;55(2):74-108.
- Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer* 2001 Oct;37 Suppl 8:S4-66.
- Parkin DM, Fernandez LM. Use of statistics to assess the global burden of breast cancer. *Breast J* 2006 Jan-Feb;12 Suppl 1:S70-80.
- Parrott S, Godfrey C, Raw M, West R, Mcneill A. Guidance for commissioners on the cost effectiveness of smoking cessation interventions. *Thorax* 1998;53(suppl 5):S2.
- Pauly MV. Risk variation and fallback insurers in universal coverage insurance plans. *Inquiry* 1992 Summer;29(2):137-147.
- Penchansky R, Thomas JW. The Concept of Access: Definition and Relationship to Consumer Satisfaction. *Med Care* 1981 Feb.;19(2):127-140.
- Pinto-Prades JL, Loomes G, Brey R. Trying to estimate a monetary value for the QALY. *J Health Econ* 2009 May;28(3):553-562.
- Pisani P, Parkin DM, Ngelangel C, Esteban D, Gibson L, Munson M, et al. Outcome of screening by clinical examination of the breast in a trial in the Philippines. *Int J Cancer* 2006 Jan 1;118(1):149-154.
- Porter P. "Westernizing" women's risks? Breast cancer in lower-income countries. *N Engl J Med* 2008 Jan 17;358(3):213-216.
- Coping with catastrophic health shocks. In: *Proceedings of the Conference on Social Protection and Poverty; 24-25 March; Washington, United States of America; 1999*.
- Przeworski A, Alvarez ME, Cheibub JA, Limongi F. *Democracy and Development Political Institutions and Well-Being in the World, 1950–1990*. Cambridge: Cambridge University Press; 2000.
- Rahman M, Haque SE, Mostofa MG, Tarivonda L, Shuaib M. Wealth inequality and utilization of reproductive health services in the Republic of Vanuatu: Insights from the Multiple Indicator Cluster Survey, 2007. *International journal for equity in health* 2011;10(1):58.
- RAND Corporation. *Family Life Surveys*. 2011; Available at: <http://www.rand.org/labor/bps/susenas.html>. Accessed May 14, 2013.

- Ranson MK. Reduction of catastrophic health care expenditures by a community-based health insurance scheme in Gujarat, India: current experiences and challenges. *Bull World Health Organ* 2002;80(8):613.
- Ravallion MM. Measuring Aggregate Welfare in Developing Countries: How Well Do National Accounts and Surveys Agree? *Rev Econ Stat* 2003;85(3):645-652.
- Rijksoverheid. Oproep alternatieve maatregelen basispakket. 2013; Available at: <http://www.rijksoverheid.nl/nieuws/2013/02/28/oproep-alternatieve-maatregelen-basispakket.html>. Accessed July/9, 2013.
- Robles SC, Galanis E. Breast cancer in Latin America and the Caribbean. *Revista Panamericana de Salud Pública* 2002;11(3):178-185.
- Rokx C, Schieber G, Harimurti P, Tandon A, Somanathan A. Health Financing in Indonesia: A Reform Read Map. 2009.
- Ruhago GM, Mujinja PG, Norheim OF. Equity implications of coverage and use of insecticide treated nets distributed for free or with co-payment in two districts in Tanzania: A cross-sectional comparative household survey. *Int J Equity Health* 2011 Jul 21;10:29.
- Russell S. Ability to pay for health care: concepts and evidence. *Health Policy Plan* 1996;11(3):219-237.
- Russell S. The economic burden of illness for households in developing countries: a review of studies focusing on malaria, tuberculosis, and human immunodeficiency virus/acquired immunodeficiency syndrome. *Am J Trop Med Hyg* 2004;71(2 suppl):147.
- Salomon JA, Carvalho N, Gutiérrez-Delgado C, Orozco R, Mancuso A, Hogan DR, et al. Intervention strategies to reduce the burden of non-communicable diseases in Mexico: cost effectiveness analysis. *BMJ. British medical journal (Clinical research ed.)* 2012 -03;344(mar02 1):e355-e355.
- Sarpong N, Loag W, Fobil J, Meyer CG, Adu-Sarkodie Y, May J, et al. National health insurance coverage and socio-economic status in a rural district of Ghana. *Tropical medicine & international health* 2010;15(2):191-197.
- Schoen C, Osborn R, Squires D, Doty MM, Pierson R, Applebaum S. How health insurance design affects access to care and costs, by income, in eleven countries. *Health Aff (Millwood)* 2010 Dec;29(12):2323-2334.
- Schoepf BG. AIDS in Africa: Structure, Agency, and Risk. In: Kalipeni E, Craddock S, Oponong JR, Gosh J, editors. *HIV&AIDS in Africa—Beyond Epidemiology* Oxford, UK: Blackwell Publishing.; 2004.
- Schoepf BG. Women, AIDS, and economic crisis in Central Africa. *Canadian journal of African studies* 1988;22(3):625.
- Schreyogg J, Stargardt T, Velasco-Garrido M, Busse R. Defining the "Health Benefit Basket" in nine European countries. Evidence from the European Union Health BASKET Project. *Eur J Health Econ* 2005 Dec;Suppl:2-10.
- Schut E, Sorbe S, Høj J. Health Care Reform and Long-Term Care in the Netherlands. 2013;no. 1010.
- Secretaría de Salud de Mexico - Dirección General de Epidemiología. Registro Histopatológico de las Neoplasias Malignas 2006. 2006.
- Seim L. Thailand: government issues compulsory licences for HIV/AIDS drugs. *HIV AIDS Policy Law Rev* 2007 May;12(1):28-29.
- Shelton JD. Is poverty or wealth at the root of HIV? *The Lancet (British edition)* 2005 -09;366(9491):1057-1058.

- Shiroiwa T, Sung YK, Fukuda T, Lang HC, Bae SC, Tsutani K. International survey on willingness-to-pay (WTP) for one additional QALY gained: what is the threshold of cost effectiveness? *Health Econ* 2010 Apr;19(4):422-437.
- Shulman LN, Willett W, Sievers A, Knaul FM. Breast cancer in developing countries: opportunities for improved survival. *J Oncol* 2010;2010:595167.
- Singletary SE, Conolly JL. Breast Cancer Staging: Working With the Sixth Edition of the AJCC Cancer Staging Manual. CA: a cancer journal for clinicians 2006 -01;56(1):37-47.
- Slamon DJ, Leyland-Jones B, Shak S, Fuchs H, Paton V, Bajamonde A, et al. Use of Chemotherapy plus a Monoclonal Antibody against HER2 for Metastatic Breast Cancer That Overexpresses HER2. *N Engl J Med* 2001 -03;344(11):783-792.
- Somkotra T, Lagrada LP. Payments for health care and its effect on catastrophe and impoverishment: experience from the transition to Universal Coverage in Thailand. *Soc Sci Med* 2008;67(12):2027.
- Sorenson C, Drummond M, Bhuiyan Khan B. Medical technology as a key driver of rising health expenditure: disentangling the relationship. *Clinicoecon Outcomes Res* 2013 May 30;5:223-234.
- Stalsberg H, Awuah B, Ibarra JA, Nsiah-Asare A. Re-establishing a surgical pathology service in Kumasi, Ghana: case report and discussion of barriers and key elements of a successful collaboration between low- and high-resource countries. *Cancer* 2008 Oct 15;113(8 Suppl):2338-2346.
- Stewart B, Kleihues P. *World Cancer Report*. 2003.
- Stivoro. vergoeding. 2013; Available at: <http://stivoro.nl/tabaksontmoediging/stoppen-met-roken/inrichtingvandezorg/vergoeding/>. Accessed July/29, 2013.
- Stolk EA, Van Donselaar G, Brouwer WBF, Busschbach JJV. Reconciliation of economic concerns and health policy: illustration of an equity adjustment procedure using proportional shortfall. *Pharmacoeconomics* 2004;22(17):1097.
- Stone ME. What is housing Affordability? The case for the Residual Income Approach. *Housing Policy Debate* 2006;17(1):151-184.
- Su TT, Kouyaté B, Flessa S. Catastrophic household expenditure for health care in a low-income society: a study from Nouna District, Burkina Faso. *Bull World Health Organ* 2006;84(1):21.
- Sun X, Jackson S, Carmichael G, Sleight AC. Catastrophic medical payment and financial protection in rural China: evidence from the New Cooperative Medical Scheme in Shandong Province. *Health Econ* 2009 -01;18(1):103-119.
- Tan-Torres Edejer T., Baltussen R, Adam T, et al editors. *WHO Guide to Cost-Effectiveness Analysis*. Geneva: World Health Organization; 2003.
- The Economist. The Economist Intelligence Unit. 2013; Available at: <http://www.eiu.com/>. Accessed 20 October, 2008.
- The Economist. Indonesia's poverty line - To make a million people unpoor. Available at: <http://www.economist.com/blogs/banyan/2011/08/indonesias-poverty-line>. Accessed October 17, 2012.
- The World Bank Group. Country groups. 2013a; Available at: <http://go.worldbank.org/D75N-0B8YU0>. Accessed July/5, 2013.
- The World Bank Group. Poverty - Data. 2013b; Available at: <http://data.worldbank.org/topic/poverty>. Accessed July/5, 2013.
- The World Bank Group. World development indicators. 2013c; Available at: <http://databank.worldbank.org/ddp/home.do>. Accessed 25 April, 2013.

- The World Bank Group. World Bank International Comparison Program 2011a; Available at: <http://go.worldbank.org/X3R0INNH80>. Accessed Feb 24, 2011.
- The World Bank Group. International Comparison Program. 2011b; Available at: [http://sitere-sources.worldbank.org/ICPEXT/Resources/ICP\\_2011.html](http://sitere-sources.worldbank.org/ICPEXT/Resources/ICP_2011.html). Accessed October 17, 2012.
- The World Bank Group. Measuring poverty at the country level. 2010; Available at: <http://go.worldbank.org/77LE4ON4V0>. Accessed January 20, 2012.
- The World Bank Group. 2008; Available at: <http://go.worldbank.org/RN07UT9ZI0>. Accessed July 5, 2013.
- The World Bank Group. Affordability and Subsidies in Urban Public Transport: What do we mean, What can be done? 2007; Policy Research Working Paper 4440 (December).
- Thomson S, Foubister T, Mossialos E. Financing health care in the European Union: challenges and policy responses. 2009.
- Tinghog G, Carlsson P. Individual responsibility for healthcare financing: Application of an analytical framework exploring the suitability of private financing of assistive devices. *Scand J Public Health* 2012 Oct 30;40(7).
- Tinghog G, Carlsson P, Lyttkens CH. Individual responsibility for what? - a conceptual framework for exploring the suitability of private financing in a publicly funded health-care system. *Health Econ Policy Law* 2010 Apr;5(2):201-223.
- Tsuchiya A. Age-related preferences and age weighting health benefits. *Soc Sci Med* 1999 -01;48(2):267-276.
- UNAIDS. Report on the Global AIDS Epidemic—A UNAIDS 10th Anniversary Special Edition. 2006.
- United Nations. The Millennium Development Goals Report 2010. 2010; En 20100604.
- United Nations Development Program. Human Development Reports. 2012a; Available at: <http://hdr.undp.org/en/reports/global/hdr2011/>. Accessed January 22, 2013.
- United Nations Development Program. The Millennium Development Goals: Eight Goals for 2015. 2012b; Available at: <http://www.undp.org/content/undp/en/home/mdgoverview.html>. Accessed March, 15, 2013.
- United Nations Development Program. Human Development Report 2007/2008. 2008; Available at: [http://hdr.undp.org/en/media/HDR\\_20072008\\_Tables.pdf](http://hdr.undp.org/en/media/HDR_20072008_Tables.pdf). Accessed 19 February, 2009.
- United Nations General Assembly. The Universal Declaration of Human Rights, article 25. 1948.
- United Nations Office of the High Commissioner for Human Rights. International Covenant on Economic, Social and Cultural Rights, article 12. 1966.
- Usher A, Cervenán A. Global Higher Education Rankings 2005. 2005.
- van de Ven WPMM. De rol van Zorgverzekeringen. In: Schut FT, F.F.H R, editors. *Economie van de gezondheidszorg*. 1e ed. Maarssen: Elsevier Gezondheidszorg; 2009.
- van de Ven WPMM, Schut FT. Universal Mandatory Health Insurance In The Netherlands: A Model For The United States? *Health affairs (Millwood, Va.)* 2008 -05;27(3):771-781.
- Van de Wetering EJ, Stolk EA, Exel van NJA, Brouwer WBF. Balancing equity and efficiency in the Dutch basic benefits package using the principle of proportional shortfall. *The European journal of health economics* 2013 -08.
- van den Boom GJM, Nsawah-Nuamah NNN, Overbosch GB. Health Care Provision and Self-Medication in Ghana. 2004.
- Van Doorslaer E, Masseria C, Koolman X. Inequalities in access to medical care by income in developed countries. *CMAJ. Canadian Medical Association journal* 2006;174(2):177-183.

- van Doorslaer E, Wagstaff A, Rutten FFH editors. Equity in the finance and delivery of health care: an international perspective. New York: Oxford University Press; 1992.
- Van Doorslaer E, O'Donnell O, Rannan-Eliya RP, Somanathan A, Adhikari SR, Garg CC, et al. Effect of payments for health care on poverty estimates in 11 countries in Asia: an analysis of household survey data. *Lancet* 2006 Oct 14;368(9544):1357-1364.
- Velasquez-De Charry LC, Carrasquilla G, Roca-Garavito S. Equity in access to treatment for breast cancer in Colombia. *Salud Publica Mex* 2009;51 Suppl 2:s246-53.
- Wagstaff A, Van Doorslaer E. Paying for health care: quantifying fairness, catastrophe, and impoverishment, with applications to Vietnam, 1993-98, Volume 1. Policy, Research working paper series 2001;WPS2715.
- Wagstaff A, Van Doorslaer E. Catastrophe and impoverishment in paying for health care: with applications to Vietnam 1993-1998. *Health Econ* 2003 Nov;12(11):921-934.
- Walsh D, Ribycki L. Symptom clustering in advanced cancer. *Support Care Cancer* 2006;14:831-5.
- Waning B, Kaplan W, King AC, Lawrence DA, Leufkens HG ea. Global strategies to reduce the price of antiretroviral medicines: evidence from transactional databases. *Bull World Health Organ* 2009;87:520.
- Ward E, Jemal A, Cokkinides V, Singh GK, Cardinez C, Ghafoor A, et al. Cancer disparities by race/ethnicity and socioeconomic status. *CA Cancer J Clin* 2004 Mar-Apr;54(2):78-93.
- Weale A. Rationing health care. *BMJ. British medical journal (Clinical research ed.)* 1998 -02;316(7129):410-410.
- Wetenschappelijke Raad voor het Regeringsbeleid. Volksgezondheidszorg. 1997.
- Whitehead CME. From Need to Affordability: An Analysis of UK Housing Objectives. *Urban Studies* 1991;28(6):871-887.
- WHO Department of Essential Health Technologies. 2005; Available at: [http://www.who.int/medical\\_devices/appropriate\\_use/en/](http://www.who.int/medical_devices/appropriate_use/en/). Accessed April 18, 2013.
- Wilf-Miron R, Galai N, Gabali A, Lewinchoff I, Tov OS, Lernau O, et al. Organizational efforts to improve quality while reducing healthcare disparities: the case of breast cancer screening among Arab women in Israel. *Qual Saf Health Care* 2010 Oct;19(5):e36.
- Williams A. Intergenerational equity: an exploration of the 'fair innings' argument. *Health Econ* 1997 Mar-Apr;6(2):117-132.
- Wingood GM, DiClemente RJ. Application of the theory of gender and power to examine HIV-related exposures, risk factors, and effective interventions for women. *Health Educ Behav* 2000 Oct;27(5):539-565.
- Wit de GW. De prijsvorming van verzekeringen. In: von Eije JH, de Bakker ACM, Kuys PHM, de Waal L, editors. Deventer: Kluwer Bedrijfswetenschappen; 1987. p. 43-56.
- World Health Organization. Breast cancer: prevention and control. 2012a; Available at: <http://www.who.int/cancer/detection/breastcancer/en/index.html>. Accessed July, 17, 2012.
- World Health Organization. Cost-Effectiveness thresholds. 2012b; Available at: [http://www.who.int/choice/costs/CER\\_thresholds/en/index.html](http://www.who.int/choice/costs/CER_thresholds/en/index.html). Accessed September 7, 2012.
- World Health Organization. Global Health Observatory. 2012c; Available at: [http://www.who.int/gho/publications/world\\_health\\_statistics/en/index.html](http://www.who.int/gho/publications/world_health_statistics/en/index.html). Accessed January 22, 2013.
- World Health Organization. Access to medicines. 2008a; Available at: <http://www.who.int/trade/glossary/story002/en/>. Accessed 22 April, 2009.
- World Health Organization. Global Burden of Disease 2004 update. 2008b.
- World Health Organization. WHO Model Formulary. 2008c; Available at: [http://www.who.int/selection\\_medicines/list/WMF2008.pdf](http://www.who.int/selection_medicines/list/WMF2008.pdf). Accessed August 27, 2009.

- World Health Organization. Public health innovation and intellectual property rights. Report of the Commission on Intellectual Property Rights, Innovation, and Public Health. 2006:134-136.
- World Health Organization. Global Burden of Disease - 2004 update. 2004a; Available at: [http://www.who.int/healthinfo/global\\_burden\\_disease/2004\\_report\\_update/en/index.html](http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html). Accessed 12 February, 2010.
- World Health Organization. WHO Medicines Strategy 2004-2007 - Countries at the core. 2004b.
- World Health Organization. World Health Survey. 2003; Available at: <http://www.who.int/healthinfo/survey/en/>. Accessed August, 8, 2011.
- World Health Organization. Global Comparative Pharmaceutical Expenditures with Related Reference Information. 2000; Health Economics and Drugs EDM Series No. 3.
- World Health Organization. Equity. Available at: <http://www.who.int/healthsystems/topics/equity/en/>. Accessed November 10, 2010.
- World Health Organization, Health Action International. Measuring medicine prices, availability, affordability and price components – 2nd edition. ; 2008.
- Xu K, Evans DB, Kawabata K, Zeramdini R. Household catastrophic health expenditure: a multi-country analysis. *The Lancet (British edition)* 2003;362(9378):111-117.
- Xu K, Ravndal F, Evans DB, Carrin G. Assessing the reliability of household expenditure data: Results of the World Health Survey. *Health policy (Amsterdam)* 2009;91(3):297.
- Zelle SG, Nyarko KM, Bosu WK, Aikins M, Niëns LM, Lauer JA, et al. Costs, effects and cost-effectiveness of breast cancer control in Ghana. *Trop Med Int Health* 2012;17(8):1031-43.
- Zotov V, Shyyan R, PATH Breast Cancer Assistance Program. Introduction of breast cancer screening in Chernihiv Oblast in the Ukraine: report of a PATH Breast Cancer Assistance Program experience. *Breast J* 2003 May-Jun;9 Suppl 2:S75-80.



# Summary

Scarcity of resources is an important element in many health care discussions. With health care costs increasing and resources being limited, scholars and policy makers in low- and middle-income countries (LMICs) as well as in high-income countries are confronted with difficult decisions on how to organize their health care systems and which treatments to reimburse (and for whom). In many LMICs, economic development leads to higher expectations of the health care systems, and increasing expenditures. In high-income countries, new medical technologies and aging populations are partly responsible for increasing and difficult to contain health care costs. In this dissertation, we focus on the issue of affordability. More specifically, we address three main questions: i) How can the affordability of health care services be measured in LMICs? ii) How can the concept of affordability inform choices regarding the benefit package of a mandatory health insurance system? iii) How can health economics help policymakers in making choices when resources are scarce? The aim of this thesis is to advance the understanding of the affordability concept in health care in LMICs and high-income countries and hence contribute to both the methodological development of methods to calculate affordability as well as their usefulness for policy makers in daily practice.

## **PART I – Affordability at the micro level in low- and middle-income countries: the example of medicine affordability.**

The first part of this thesis focuses on the affordability of health care in LMICs. Affordability in these countries is addressed from the individual perspective as in the majority of LMICs a health insurance system is not in place and the majority of patients have to pay for their treatments out-of-pocket. Therefore, the question we ask in this part is whether an individual patient can afford to pay for a treatment, i.e. micro affordability. In Chapter 2 of this dissertation we consider two methods that can be used to calculate the affordability of medicines for individual patients. The catastrophic method quantifies the proportion of the population whose resources would be catastrophically reduced by spending on a given medicine. Expenditures are labeled as 'catastrophic' when they exceed a certain percentage of the available income. The impoverishment method estimates the proportion of the population that would be pushed below a relevantly defined poverty line due to procuring a given medicine. The abovementioned percentage and poverty line therefore constitute the thresholds against which affordability is measured. The gold standard of calculating catastrophic payment and impoverishment rates is using household level data. However, in many LMICs these data are not gathered regularly. This not only limits the opportunity to calculate the proportion of the population at risk of



or experiencing catastrophic payments or impoverishment, but also the evaluation of policies aimed to improve the affordability of medicines. Furthermore, because these household level data are not regularly available, comparing the affordability of medicines both over time and across countries is limited. The use of aggregated data can address some of these issues. We illustrate this with an application of these two methods using aggregated data. This provides more insight to policymakers regarding affordability of health care.

In chapter 3 of this thesis, we apply the impoverishment method with aggregated data across a sample of 16 countries to calculate the affordability of 4 essential medicines. Comparing medicine prices to people's available income and using poverty lines of US\$1.25 and US\$2.00 we show that a large proportion of the population in these countries is at risk of becoming impoverished if they have to procure one of these medicines. To improve this situation we recommend policy makers to promote the use of quality-assured low-priced generic versions of these medicines and, where possible, implement health insurance systems.

The concept of affordability is normative in nature, i.e. what one deems affordable varies across people. Calculating the affordability of medicines, or any other commodity, requires information from three sources: i) the price of this commodity, ii) income(s) and iii) a threshold of unacceptable burden. Whereas the first two are taken from data sources, the latter essentially involves an arbitrary, normative choice. In chapter 4, using the example of medicine purchases in Indonesia, we study the impact of using different thresholds both for the catastrophic payment and impoverishment methods. As expected, we show the impact of the thresholds chosen to considerably influence the catastrophic payment and impoverishment rates. Consequently, we argue that it is important to further standardize methods and thresholds in applied research. This increases the comparability of results and facilitates sound assessments of affordability, which policy makers need to improve the affordability and access to health care.

## **PART II – Affordability at the macro level in a developed country: delineating entitlements in system of (social) health insurance.**

In high-income countries where systems of (social) health insurance are functioning, many governments have taken steps to control increasing costs. Besides implementing deductibles and co-payment arrangements, the entitlements of the basic benefit packages are also critically examined. Governments are responsible for ensuring that people's mandatory financial contributions are employed in a responsible manner and, at the same time, that the financial accessibility of their health care system is

guaranteed. In the Netherlands, the Dutch Healthcare Insurance Board (CVZ) is responsible for advising the Minister of Health about the content of the basic benefit package. CVZ uses the criteria of *Necessity, Effectiveness, Efficiency* and *Feasibility* to determine if an intervention should be reimbursed. The operationalization of these criteria is not finished, however. In chapter 5 we aim to take forward the operationalization of the *necessity of insurance* (NoI-) element which, together with the concept of *disease burden*, forms the *Necessity* criterion. The NoI-element asks *whether it is socially necessary or appropriate to insure an intervention*. The operationalization of the NoI-element is not finished yet, both in terms of content as well as process. We introduce a framework which aims to help the assessors of interventions at CVZ to systematically evaluate all important considerations encompassed in the NoI-element. The framework poses 8 questions that are grouped in the themes of *health insurance as an instrument* and *financial accessibility*. The framework thus provides guidance, structure and transparency regarding the NoI element.

### **PART III – Health economics at the macro level in low- and middle-income countries: choices in breast cancer and HIV/AIDS.**

Besides measuring affordability, health economic techniques can be used to help inform the difficult decisions that policy makers are confronted with when deciding on how to allocate scarce resources. The final three chapters of this dissertation report on the application of some of these techniques in the fields of breast cancer and HIV/AIDS.

Breast cancer incidence and prevalence are increasing in LMICs. Although they are still much lower than in high-income countries, the majority of breast cancer mortality occurs in LMICs. In chapter 6 we calculate the most cost-effective policy options for treating breast cancer in both Costa Rica and Mexico. Local experts indicated the most urgent policy questions in both countries to be the age-groups that should be targeted for screening and whether treating Her2/NEU+ patients with Trastuzumab (Herceptin™) was cost-effective. Using WHO-choice methodology, for both Mexico and Costa Rica, we calculated the cost-effectiveness of the current breast cancer programs and 18 other treatment scenarios by comparing them with a null scenario in which no care is delivered. According to WHO-choice methodology effects were measured in disability-adjusted life years (DALYs) averted. Costs were assessed in 2009 United States Dollars (US\$). To the extent available, analyses were based on locally obtained data.

We show that the current strategy of treating breast cancer in stages I to IV at a 80% coverage level seems to be the most cost-effective in Costa Rica with an incremental cost-effectiveness ratio (ICER) of US\$4,739 per DALY averted. Our results

show that in Costa Rica a biennial clinical breast examination (CBE) screening program (95% coverage) could double the number of DALYs averted. With an ICER of US\$5,964/DALY, this can still be considered (very) cost-effective. Our analyses indicate furthermore that a mass-media awareness raising program (MAR) maybe the most cost-effective for Mexico (ICER US\$5,042/DALY). Biennial mammography screening for women 50-70yrs (ICER US\$12,718/DALY), adding trastuzumab (ICER US\$13,994/DALY) or screening women 40-70yrs biennially plus trastuzumab (ICER US\$17,115/DALY) also improve population health but are less cost-effective options.

For improving their current breast cancer control programs, our analysis suggests that both Costa Rica and Mexico would benefit from implementing strategies that advance early detection. For these countries, a mass-media awareness raising program and/or a CBE screening program coupled with treatment of all stages and careful monitoring and evaluation could be feasible options. If these strategies are implemented, the provision of breast cancer diagnostic, referral, treatment and, when possible, basic palliative care services is essential and should be facilitated simultaneously. A gradual implementation of early detection programs should give the respective Ministries of Health the time to negotiate the required budget, train the required human resources and understand possible socioeconomic barriers to uptake. Also, these programs require several organizational, budgetary and human resources, and the accessibility of breast cancer diagnostic, referral, treatment and palliative care facilities should be improved simultaneously.

In chapter 7 we report on the equity situation of breast cancer care provided in Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana. Using the same mathematical model as used in chapter 6 we analyze in which socio-economic groups most DALYs are averted when being treated at KATH. We calculate the DALYs averted from differences in stage distributions. Our results show that while patients from higher SES-quintiles sooner present themselves at the hospital, their stage distribution is not significantly different from patients of lower SES-quintiles. Hence, we find no significant association between SES and health outcomes at KATH, although this might be due to a small sample size. As over 75% of the patients present at KATH with late stage disease and in Ghana the geographical coverage of breast cancer services is low, improving awareness regarding and access to breast cancer services for patients seems the best option to improve breast cancer outcomes.

Scholars have shown levels of HIV-prevalence to be influenced by, among others, levels of education, prosperity, health care spending, gender equity, religious affiliation etc. In chapter 8 we try to explain variations in levels of HIV-prevalence over a 5-year span by looking at these variables jointly. We find strong support for our

expectation that gender equity influences HIV-prevalence. Gender equity matters both in terms of the level as well as in the change of HIV-prevalence. Of course, this finding in itself does not justify the reallocation of resources to interventions focusing on improving gender equity as these might not provide value for money, i.e. may not be cost-effective.



# Samenvatting

Beperkte financiële middelen zijn een belangrijk onderwerp binnen veel discussies over de gezondheidszorg. Beleidsmakers in zowel lage- en midden-inkomenslanden alsook hoge-inkomenslanden zien de kosten in de gezondheidszorg stijgen. Omdat de beschikbare financiële middelen beperkt zijn worden zij geconfronteerd met moeilijke keuzes over hoe hun gezondheidszorgsysteem te organiseren en welke behandelingen wel en niet te vergoeden. In veel lage- en midden-inkomenslanden leidt economische ontwikkeling tot hogere verwachtingen van het gezondheidszorgsysteem, wat gepaard gaat met een toenemende vraag en hogere kosten. In hoge-inkomenslanden zijn nieuwe medische technologieën en vergrijzende populaties gedeeltelijk verantwoordelijk voor de immer stijgende kosten van de gezondheidszorg.

Het onderwerp van dit proefschrift is het thema betaalbaarheid in de gezondheidszorg. Meer specifiek probeert het een antwoord te formuleren op drie vragen: i) Hoe kan de betaalbaarheid van gezondheidszorg voorzieningen in lage- en midden-inkomenslanden gemeten worden? ii) Hoe kan het concept van betaalbaarheid keuzes informeren met betrekking tot het verzekerde basispakket in een gezondheidszorg stelsel met een verzekeringsplicht? iii) Hoe kan gezondheidseconomie beleidsmakers helpen met het maken van keuzes in situaties waar de beschikbare financiële middelen beperkt zijn?

## **DEEL I – Betaalbaarheid op het micro niveau in lage- en midden-inkomenslanden: de betaalbaarheid van medicijnen.**

Het eerste deel van dit proefschrift focust op betaalbaarheid van gezondheidszorg in lage- en midden-inkomenslanden. Betaalbaarheid in deze landen wordt benaderd vanuit een individueel perspectief omdat in het merendeel van deze landen mensen, bij gebrek aan een verzekeringssysteem, zelf hun medicijnen moeten betalen. De vraag die in dit deel gesteld wordt is dan ook of een individuele patiënt zich een behandeling met medicijnen kan veroorloven; betaalbaarheid op micro niveau. Hoofdstuk 2 van dit proefschrift beschrijft twee methodes die gebruikt kunnen worden om de betaalbaarheid van medicijnen voor individuele patiënten te berekenen. De methode van catastrofale betalingen kwantificeert de proportie van de bevolking wiens inkomen met meer dan een vooraf bepaald percentage zal afnemen wanneer men medicijnen dient te kopen. In deze benadering worden uitgaven die meer dan dit percentage van het totale beschikbare inkomen omvatten als catastrofaal beschouwd. De armoede methode schat de proportie van de bevolking die beneden een armoedegrens wordt gedrukt door uitgaven aan medicijnen. Het percentage en de armoedegrens in de methodes zijn de drempelwaardes waartegen betaalbaar-

heid afgemeten wordt. De gouden standaard voor het berekenen van percentages van respectievelijk catastrofale betalingen en de proportie van de bevolking die onder een armoedegrens wordt gedrukt, is het gebruik van huishoudenquêtes. In lage- en midden-inkomenslanden komen deze enquêtes echter niet regelmatig beschikbaar, wat de mogelijkheden om beide methodes toe te passen aanzienlijk verkleint. Een ander gevolg is dat het vergelijken van de betaalbaarheid van medicijnen, zowel over de tijd alsook tussen landen, beperkt is. In dit proefschrift ontwikkelen we alternatieve operationalisaties van de twee methodes die enkele van deze beperkingen wegnemen. Gebruik makend van geaggregeerde data laten we zien dat het gebruik van de twee alternatieve operationalisaties met kwalitatief goede geaggregeerde data betrouwbare resultaten geven voor beleidsmakers om hun beleid op te baseren.

In hoofdstuk 3 van dit proefschrift gebruiken we de armoede methode met geaggregeerde data om in een selectie van 16 landen de betaalbaarheid van 4 essentiële medicijnen te berekenen. Door medicijnprijzen te vergelijken met het beschikbaar inkomen van mensen en armoedegrenzen van US\$1.25 US\$2.00 laten we zien dat grote groepen van de bevolking in deze landen het risico lopen in armoede gedrukt te worden wanneer ze deze medicijnen moeten aanschaffen. Om deze situatie te verbeteren adviseren we beleidsmakers om het gebruik van generieke medicatie van een goede kwaliteit te promoten en waar mogelijk een nationaal systeem met gezondheidszorgverzekeringen op te zetten.

Het concept 'betaalbaarheid' is van nature normatief: wat iemand betaalbaar acht verschilt. Voor het berekenen van de betaalbaarheid van medicijnen, of een ander goed, is informatie van drie parameters nodig: i) de prijs van het goed, ii) inkomensgegevens en iii) een drempelwaarde van onacceptabele last. Waar de eerste twee parameters uit gegevensbronnen worden genomen, behelst de drempelwaarde in feite een arbitraire keuze. Als zodanig ligt het ten grondslag aan het normatieve karakter van het betaalbaarheid concept. In hoofdstuk 4 maken we gebruik van medicijnaankopen in Indonesië om de impact van de drempelwaarde op zo de catastrofale betalingen alsook de armoede methode te bestuderen. We laten zien dat de keuze van verschillende drempelwaardes de uitkomsten van beide methodes sterk beïnvloeden. Derhalve beargumenteren we dat het van belang is om deze methodes, en het gebruik van drempelwaardes in toegepast onderzoek, verder te standaardiseren om zo de vergelijkbaarheid van de resultaten te vergroten en beleidsmakers te helpen bij het ontwikkelen van beleid gericht op het verbeteren van de betaalbaarheid van de gezondheidszorg.

## **DEEL II – Betaalbaarheid op macro niveau in een hoog inkomensland: het afbakenen van aanspraken in sociale gezondheidszorgsystemen.**

In hoog inkomenslanden waar op nationaal niveau (sociale) gezondheidszorgsystemen geïmplementeerd zijn, nemen veel overheden maatregelen om de immer stijgende kosten van deze systemen te beperken. Naast het invoeren van eigen risico's en eigen betalingen, wordt ook de omvang van het verzekerde basispakket kritisch bestudeerd. Overheden zijn immers verantwoordelijk er voor te zorgen dat de verplichte bijdragen van verzekerden op een verantwoordelijke manier ingezet worden. Daarnaast dient ook de financiële toegang tot het gezondheidszorgsysteem gewaarborgd te blijven. In Nederland adviseert het College voor Zorgverzekeringen (CVZ) de Minister van Volksgezondheid, Welzijn en Sport over de inhoud van het basispakket. Het CVZ gebruikt de criteria van *Noodzakelijkheid*, *Effectiviteit*, *Doelmatigheid*, en *Uitvoerbaarheid* om te peilen of een interventie verzekerde zorg is. Echter, de operationalisatie van deze criteria is nog niet afgerond. In hoofdstuk 5 proberen we de operationalisatie van het 'noodzakelijk te verzekeren' (NtV) element verder te brengen. Samen met het concept *ziektelast* maakt NtV deel uit van het *Noodzakelijkheid* criterium. Onder het NtV-element wordt onderzocht of het maatschappelijk bezien nodig of aangewezen is om een zorginterventie te verzekeren. In het licht van kritisch bestuderen van de omvang van het basispakket staat het NtV-element in de belangstelling van beleidsmakers. De operationalisatie van het NtV-element is nog niet voltooid, zowel op het gebied van de inhoud alsook wat betreft het proces. We introduceren een kader dat tot doel heeft de beoordelaars van het CVZ te helpen bij het systematisch evalueren van alle belangrijke overwegingen die binnen het NtV-element vallen. Het kader bestaat uit 8 vragen die gegroepeerd zijn in twee thema's: *zorgverzekering als instrument* en *financiële toegankelijkheid*. De vragen functioneren als richtsnoer en het beantwoorden ervan biedt structuur en transparantie in de discussies die het CVZ over dit onderwerp voert.

## **DEEL III – Gezondheidseconomie op macro niveau in lage- en midden inkomenslanden: keuzes in borstkanker en HIV/AIDS.**

Technieken uit de gezondheidseconomie kunnen beleidsmakers informeren wanneer zij zich voor moeilijke keuzes gesteld zien staan. De laatste drie hoofdstukken van dit proefschrift rapporteren over onderzoeken op het gebied van HIV/AIDS en borstkanker waar enkele van deze technieken zijn toegepast.

De incidentie en prevalentie van borstkanker stijgen in lage- en midden inkomenslanden. Hoewel deze nog steeds veel lager zijn dan in hoge inkomenslanden, vinden de meeste sterfgevallen als gevolg van borstkanker plaats in lage- en midden inkomenslanden. In hoofdstuk 6 berekenen we de meest kosten-effectieve beleidsopties



voor het detecteren en behandelen van borstkanker in Costa Rica en Mexico. De belangrijkste beleidsvragen van lokale experts betroffen de leeftijdsgroepen die gescreend zouden moeten worden en of het gebruik van Trastuzunab (Herceptin™) bij Her2/NEU+ patiënten kosten-effectief was. Gebruikmakend van WHO-CHOICE methodologie berekenen we de kosten-effectiviteit van 19 behandelings-scenarios door deze te vergelijken met een 'nul'-scenario waarin geen borstkanker zorg wordt geleverd. In lijn met de WHO-CHOICE methodologie zijn effecten gemeten in voor beperkingen gecorrigeerde levensjaren, zogenaamde DALYs (Disability Adjusted Life Years). Kosten zijn uitgedrukt in 2009 Amerikaanse dollars. Voor zover mogelijk zijn de analyses uitgevoerd op basis van lokaal verkregen data.

We laten zien dat de huidige strategie om borstkanker in stadia I tot en met IV te behandelen met een landelijke dekking van 80% in Costa Rica het meest kosten-effectief lijkt te zijn met een incrementele kosten-effectiviteits ratio (ICER) van US\$4,739/DALY. Onze resultaten laten zien dat een tweejaarlijks klinisch borstonderzoek (dekking 95%) het totale aantal vermeden DALYs kan verdubbelen.

Met een ICER van US\$5,964/DALY, is dit nog steeds kosten-effectief. Onze analyse toont aan dat een programma gericht op het verbeteren van het bewustzijn bij mensen over borstkanker via de media het meest kosten effectief kan zijn voor Mexico (ICER US\$ 5,042/DALY). Tweejaarlijkse mammografie screening voor vrouwen tussen 50 -70 jaar (ICER US\$12,718/DALY), het hieraan toevoegen van Trastuzumab (ICER US\$13,994/DALY) en vervolgens het uitbreiden van het programma naar vrouwen tussen 40 -70 jaar (ICER US\$17,115/DALY) leidt ook tot meer vermeden DALYs. Deze opties zijn minder kosten-effectief en alleen mogelijk wanneer er meer (financiële) middelen beschikbaar zijn.

Afhankelijk van het beschikbare budget bevelen we Costa Rica en Mexico aan om programma's gericht op het vergroten van het bewustzijn van borstkanker via de media, klinisch borstonderzoek of mammografie in te voeren. Een geleidelijke implementatie van programma's gericht op vroege detectie zou de Ministeries van Volksgezondheid in beide landen de tijd moeten geven om het benodigde budget bij elkaar te krijgen, het benodigde personeel op te leiden en mogelijke sociaal economische barrières in kaart te brengen en te slechten. Omdat het bewijs van de effectiviteit van de interventie gericht op het verbeteren van het bewustzijn bij mensen over borstkanker via de media onzeker is, is voorzichtigheid geboden bij het interpreteren van deze resultaten. Om de onderzochte programma's te implementeren dienen voldoende organisatorische, budgetaire and personele middelen beschikbaar gesteld te worden. Het verbeteren van de toegang tot diagnostiek, verwijzing, behandel en palliatieve voorzieningen is noodzakelijk zodat vrouwen met positieve screeningsresultaten ook daadwerkelijk behandeld kunnen worden.

In hoofdstuk 7 rapporteren we over de billijkheid van de verdeling van uitkomsten in borstkanker behandelingen in Komfo Anokye Teaching Hospital (KATH) in Ghana. We maken gebruik van hetzelfde wiskundige model als in hoofdstuk 6, en analyseren welke inkomensgroepen in de Ghanese bevolking de meeste 'Disability Adjusted Life Years' (DALYs) vermijden wanneer ze in KATH behandeld worden. Het aantal DALYs is het aantal gezonde levensjaren dat een bevolking vermijdt als gevolg van ziekte of vroegtijdig overlijden. We berekenen de vermeden DALYs vanuit hoe de tumoren in verschillende inkomensgroepen verdeeld zijn over de ziektestadia van borstkanker, de stadiumdistributie. Onze resultaten laten zien dat hoewel patiënten uit een hogere inkomensgroep sneller naar het ziekenhuis komen, hun stadiumdistributie niet significant afwijkt van patiënten uit lagere inkomensgroepen. We vinden dus geen significante associatie tussen inkomensgroepen en behandeluitkomsten in KATH, hoewel dit een gevolg kan zijn van een kleine steekproef. Omdat meer dan 75% van de patiënten KATH binnenkomen met vergevorderde borstkanker en in Ghana de geografische beschikbaarheid van borstkanker voorzieningen laag is, lijkt het mensen bewust maken van borstkanker via de media en het de toegang tot borstkanker voorzieningen verbeteren de beste optie om de uitkomsten van borstkankerbehandelingen te verbeteren.

Wetenschappers hebben aangetoond dat HIV-prevalentie beïnvloed wordt door onder andere, het opleidingsniveau, (economische) welvaart, uitgaven aan de (publieke) gezondheidszorg, de mate van gelijkheid tussen mannen en vrouwen, religieuze affiliatie etc. In hoofdstuk 8 proberen we over een periode van 5 jaar verschillen in HIV-prevalentie in sub-Sahara Africa te verklaren door naar alle eerdergenoemde variabelen tegelijk te kijken. De uitkomsten steunen onze hypothese dat de gelijkheid tussen mannen en vrouwen van invloed is op HIV-prevalentie. Gelijkheid tussen mannen en vrouwen doet er toe zowel in termen van het absolute niveau van HIV-prevalentie alsook bij de verandering van HIV-prevalentie over 5 jaar. Natuurlijk rechtvaardigt deze bevinding niet direct een herallocatie van middelen naar het verbeteren van de gelijkheid tussen mannen en vrouwen zolang niet bekend is of ze kosten-effectief zijn.



# Dankwoord

Het schrijven van het dankwoord bij een proefschrift is een bijzonder moment. Het resultaat van vier jaar werken wordt afgesloten met wellicht het enige stukje dat je naasten helemaal zullen lezen. Het is een mooie tijd geweest, waarin ik bijzondere mensen heb ontmoet en waarin het opdoen van kennis en persoonlijke groei hand in hand zijn gegaan. Dat dit werk er nu ligt is mede te danken aan de inzet en steun van velen. Enkele mensen in het bijzonder wil ik hier bedanken.

Allereerst mijn promotoren Werner Brouwer en Frans Rutten. Beste Werner, tijdens mijn tijd aan de Erasmus Universiteit is jouw begeleiding onmisbaar geweest. Zowel bij het schrijven van mijn masterscriptie maar vooral bij het proces dat tot dit proefschrift heeft geleid. Voor de manier waarop jij tussen verschillende onderwerpen schakelt en het overzicht bewaart heb ik grote bewondering. En dat alles met humor en relativeringsvermogen. Het maakte onze gesprekken, die de inhoud van dit proefschrift soms ver te buiten gingen, erg plezierig. Hartelijk dank daarvoor.

Mijn 2<sup>e</sup> promotor Frans Rutten. Beste Frans, van 2<sup>e</sup> lezer bij mijn masterscriptie tot 2<sup>e</sup> promotor; de hele rit was je erbij. Dankjewel dat je me de vrijheid hebt gegeven het door Susan G. Komen for the Cure gefinancierde borst kanker project naar eigen goeddunken in te vullen. Je vertrouwen dat het goed zou komen wanneer ik alleen naar het buitenland vertrok, en je steun wanneer het tegen zat, waardeer ik zeer.

De leden van de promotiecommissie wil ik bedanken voor het bestuderen van mijn proefschrift en het opponeren bij de verdediging daarvan. Mijn co-auteurs ben ik dank verschuldigd voor hun bereidheid hun kennis en kunde met mij te delen. Ellen en Elly, het lijkt geen twijfel dat zonder jullie hulp hoofdstukken 2 t/m 5 er nooit waren gekomen. Sten, dankjewel voor de manier waarop je me wegwijs hebt gemaakt in het borstkanker model en mijn vragen daarover steeds beantwoord hebt. De vijf weken die we samen in Ghana gewerkt en gereisd hebben zal ik niet snel vergeten!

De mensen bij het CVZ wil ik bedanken voor de prettige samenwerking binnen het Academia project. I am grateful to Richard Laing, Alexandra Cameron and Margaret Ewen for providing me with the opportunity to work on the Health Action International & World Health Organization medicine prices and availability project. I could not have imagined that what started as my mastersthesis eventually would become an important part of my PhD. A word of thanks also for David Lowery; his enthusiasm and patience in supervising my first master's thesis in Public Administration fostered my interest in research. I am happy our paper on HIV/AIDS is part of this dissertation.

Para mis colegas en Costa Rica y México; muchas gracias por su hospitalidad durante mis visitas. ¡No los voy a olvidar! De collega's bij het iBMG wil ik hartelijk bedanken voor de prettige werksfeer. Van de gezamenlijke lunches, het invullen van de voetbalpoule en de ROPA-run tot het bezoeken van verschillende congressen; ik heb ervan genoten.

Mijn paranimfen. Ernest, als broers hebben we veel meegemaakt maar behalve dat ik regelmatig op reis ging, heb je niet heel veel over mijn werk meegekregen. Ik ben erg blij dat je deze dag als paranimf met me kan beleven. Koen, dankjewel voor je steun en vriendschap in al die jaren. Dat je vandaag mijn paranimf bent vind ik heel bijzonder.

Mijn ouders. Lieve pap en mam, dat ik hier na al die jaren mag staan is iets wat weinigen voor mogelijk hadden gehouden. Bedankt voor de manier waarop jullie mij, ieder op je eigen manier, onvoorwaardelijk gesteund hebben.

De laatste loodjes wegen het zwaarst, daar is dit proefschrift geen uitzondering op. Dass es mit dir ein bisschen einfacher war und sehr viel mehr Spaß gemacht hat, ist klar für mich. Liebe Katja, es ist unglaublich dass bei dir meine Macken wirklich Special Effects sind. Vielen Dank für alles.

# PhD portfolio

## COURSES

- Training Tutor Vaardigheden in Probleem gestuurd onderwijs (Erasmus University Rotterdam - 2011)
- Medical Demography Fundamentals & Applications (NIHES - 2011).
- Advanced Economic Evaluation (Erasmus University Rotterdam - 2011)
- Panel / Longitudinal Data Analysis (University College London - 2010)
- Klaar in vier jaar (Erasmus University Rotterdam - 2010)
- Applied Health Econometrics (Erasmus University Rotterdam - 2010)

## TEACHING

- Lecturing and supervising working groups in Bachelors course "Verdelingsvraagstukken". (2010 - 2013)
- BSc Thesis supervisor. (2011 - 2013)
- MSc Thesis co-reader - Master Health Economics Policy and Law. (2010 - 2012)
- Diploma Course International Health and Policy Evaluation. (2010 - 2011)

## CONFERENCES

- 8<sup>th</sup> World Congress on Health Economics. 2011. Toronto, Canada. (Poster + short oral)
- 3<sup>rd</sup> Low Lands Health Economists' Study Group. 2011. Soesterberg, The Netherlands. (Attendent)
- Global Summit on International Breast Health: Optimizing Healthcare Delivery. 2010. Chicago, U.S.A. (Oral presentation)
- European Conference on Health Economics. 2010. Helsinki, Finland. (Oral Presentation)
- 2<sup>nd</sup> Low Lands Health Economists' Study Group. 2010. Egmond aan Zee, The Netherlands. (Attendent)
- 12<sup>th</sup> annual European congress of the International Society for Pharmacoeconomics and Outcomes Research. 2009. Paris, France. (Poster)

- 1<sup>st</sup> Low Lands Health Economists' Study Group. 2009. *Berg en Terblijt*, The Netherlands. (Attendent).

## OTHER PUBLICATIONS

- Zelle SG, Nyarko KM, Bosu WK, Aikins M, Niëns LM, Lauer JA, Sepulveda CR, Hontelez JAC, Baltussen R,. "Costs, effects and cost-effectiveness of breast cancer control in Ghana" *Tropical Medicine & International Health*, 2012 17(8): 1031-1043.
- Harford JB, Otero IV, Anderson BO, Cazap E, Gradishar WJ, Gralow JR, Kane GM, Niëns LM, Porter PL, Reeler AV, Rieger PT, Shockney LD, Shulman LN, Soldak T, Thomas DB, Thompson B, Winchester DP, Zelle SG, Badwe RA. Problem solving for breast health care delivery in low and middle resource countries (LMCs): consensus statement from the Breast Health Global Initiative. *The Breast Journal* 2011 17(2): 1-10.

## Curriculum Vitae

Laurens M. Niëns was born in Weert on February 15th, 1983. After finishing high school in 2001 he started his studies at Leiden University, where he obtained his MA in Public Administration. He continued his education by enrolling in the Health Economics Policy and Law masters at the institute for Health Policy and Management (iBMG) at Erasmus University Rotterdam. For his graduation project he organized internships at Health Action International (HAI) and the World Health Organization (WHO). In a joint WHO/HAI project on Medicine Prices and Availability Laurens developed alternative applications of methods to estimate the affordability of medicines.

After graduating in 2009 he started working for iBMG as a junior researcher. Besides continuing to work on measuring the affordability of medicines in low- and middle-income countries, he studied the cost-effectiveness of various breast cancer interventions in central- and south-America together with Radboud University Nijmegen and the World Health Organization. Sponsored by the Susan G. Komen for the Cure foundation, this project led him to organize and hold workshops in Costa Rica, Mexico and Brazil. In Ghana Laurens set up an equity study in breast cancer outcomes that was sponsored by the same foundation.

During his time at iBMG Laurens taught in a bachelors' course on rationing in health care, both as an instructor and lecturer. He also supervised several students with writing their bachelors' thesis and taught on the Principles of Economic Evaluation in the Diploma Course program on "International Health and Policy Evaluation", as jointly organized by iBMG, the International Institute of Social Studies (ISS) and the Department of Public Health (MGZ) at the Erasmus Medical Center.



