# **iDSI Methods Working Group report**

# Human resource constraints and the methods of economic

# evaluation of health care technologies

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This report was produced as part of the Research arm of the International Decisions Support Initiative (iDSI); in a collaboration between the University of Glasgow, the London School of Hygiene and Tropical Medicine, Erasmus University, Rotterdam, and the Centre for Health Economics, University of York.

In the first phase of iDSI (2014-2016), Methods Working Groups were established to investigate three areas of economic evaluation for which additional methods guidance for analysts and policymakers in low- and middle-income countries was deemed particularly valuable. These linked directly to specific Principles for the practice of economic evaluation detailed in the iDSI Reference Case. The three research areas were identified by policymakers in low- and middle-income countries as being particularly challenging and requiring additional methods guidance in order to support the realisation of their corresponding Reference Case Principles.

This report details the findings from the investigation into reflecting non-budgetary constraints in economic evaluation - linked to Principle 10: Impact on Other Constraints and Budget Impact - The impact of implementing the intervention on the health budget and on other constraints should be identified clearly and separately

Additional information about the findings from the Methods Working Group can be viewed at: <u>www.idsihealth.org/knowledge\_base</u>.

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#### Summary

Health economic evaluations aim to inform decision-making about new health care technologies in order to make more efficient use of scarce resources. In order to maximize the usefulness of health economic evaluations it is important to take into account local constraints the decision maker faces. Although the starting point for economic evaluations is that resources are scarce and thus that there is a limit to what can be spend on health care, other constraints besides the health care budget might be relevant in this context. One particular type of constraints that might be relevant for health economic evaluations are human resource constraints (HRC). The goal of this report is to develop guidance on how to incorporate, present and reflect upon HRC in economic evaluations. To achieve this goal we set up a theoretical model describing the optimal allocation of the health care budget and conducted a literature review.

From the theoretical model we derived that HRC imply that the health gains of increasing the labour budget by one unit are higher than that of increasing other budgets on health care spending. Thus, if there are HRC, it is not only the estimation of the ICER that is influenced but also the estimate of the value of what is displaced. In other words, the decision rules are impacted. From the literature review we concluded that although HRC are recognized as an important problem in economic evaluations, researchers usually ignore HRC in the estimation of the ICER and fail to discuss issues with respect to opportunity costs. Based on our theoretical model and review of the literature we recommend that:

- Estimates of costs and benefits of health care technologies should incorporate HRC;
- Researchers should focus less on estimating and presenting ICERs and present more disaggregated results;
- In the presence of HRC opportunity costs need to be discussed explicitly;
- Future research should focus on better empirical estimates of opportunity costs reflecting HRC;
- In the absence of good empirical estimates of opportunity cost reflecting HRC, simple models and rules of thumb can be used to improve policy recommendations.

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## 1. Introduction

Health economic evaluations aim to inform decision-making about new health care technologies in order to make more efficient use of scarce resources (Drummond et al., 2005). They normally present incremental costs and health benefits caused a new health care technology if this were to be implemented. In order to maximize the usefulness of health economic evaluations it is important to take into account local constraints the decision maker faces. Although the starting point for economic evaluations is that resources are scarce and thus that there is a limit to what can be spent on health care, other constraints besides the health care budget might be relevant in this context. Although in the long run many constraint can (in theory) be solved by a more efficient allocation of resources, ignoring local constraints in economic evaluation might seriously hamper the usefulness and credibility of economic evaluations in health care (Smith et al., 2014). In the short-run, there are numerous constraints involved, consisting of supply-side, demand-side and healthcare system constraints. Supply-side constraints include lack of facilities, workforce and malpractice of providers whereas demand-side constraints mainly involve obstacles of access to healthcare, such as physical barriers (infrastructure), financial barriers, and cultural barriers (including awareness and knowledge). Apart from supply- and demand-side constraints, healthcare system constraints are relevant as well. They are related to the policy level, including legislation, regulation and priority setting, etc. These constraints might not only influence the estimation of costs and effects of interventions but also how optimal decisions conditional on those estimates should be made. Therefore, it is of crucial importance, to develop guidance for both researchers and decision makers how to take into account additional constraints when estimating, presenting and interpreting the results of economic evaluations.

One particular type of constraints that might be relevant for health economic evaluations are human resource constraints (HRC). This is especially the case in settings of low-middle income countries (LMIC) where there is a smaller and less skilled health workforce compared to high income countries (World health organization, 2006). In LMIC there is often a lack of supply of skilled doctors and nurses which might have a big influence on the costs and health effects of delivering a particular health care technology (Fulton et al., 2011). Increasing the size and skills of workforce is often not that easy (Wyss, 2004). For instance, raising wages to increase the workforce in low income countries might of limited success as it is difficult to compete with wages in Western countries (Robinson et al., 2008). Therefore, alternative strategies have been pursued to improve skills and size of workforce in order to improve the delivery of health care technologies different strategies such as for instance task shifting. The default decision rules of cost effectiveness analyses are derived from an optimization problem with only one constraint: the budget (Fulton et al., 2011). The theory behind this is that most constraints can be solved and the only relevant constraint in the long run is the health care budget. As HRC can be persistent and difficult to solve in some settings, the rather abstract long run view typically taken in cost effectiveness in which the only constraint is the health care budget might not be the most appropriate view (Adang, 2008; Van de Watering et al., 2012). In case of multiple constraints, mathematical programming may be needed to solve the optimization problem. A drawback of mathematical programming is that the information needs and analytical capabilities for these techniques are substantial (see for case studies Epstein et al, 2007; Feenstra et al, 2011). Furthermore, decision rules derived from such an approach become much more complex than the standard decision rules of cost effectiveness analysis (Stinnett and Paltiel, 1996).

Although economic evaluations in LMIC are more frequently conducted nowadays and issues of constraints have been recognized, little attention has been paid to how HRC might complicate the use of economic evaluations as usually practiced. The goal of this report is to develop guidance on how to incorporate, present and reflect upon HRC in economic evaluations. As a starting point we take the most popular form of economic evaluation in which costs and benefits of individual interventions are estimated and compared to a threshold level of cost effectiveness. The results of such incremental analyses are used to inform decision makers who usually take many constraints as given. This should be distinguished from generalized cost-effectiveness as proposed by the WHO (Murray et al. 2000) or so-called 'zero-based' economic evaluation which aims to define an entire health benefits package (Smith et al. 2014). These forms of economic evaluations take more a long term view and are usually directed at decision makers at a higher level. First, in the following chapter, we will present a definition of HRC and present the consequences of HRC on the estimation of the ICER and the decision rules of cost effectiveness analysis. In Chapter 3, we explore to what extent human resource constraints are taken into account in health economic evaluations and confront this with the insights developed in Chapter 2. Finally, Chapter 4 concludes with recommendations.

# 2. Theoretical framework

In this report, a health care perspective is taken implying that potential consequences of health care technologies outside the health care sector (e.g. productivity gains, informal care, and changes in non-medical consumption) and utility gains not captured in the QALY (e.g. utility losses of leisure forgone and utility gains of changes in non-medical consumption) are, not to get too complex at this stage, disregarded. However, insights that we gain in this chapter also apply if the perspective is broadened to a wider societal perspective. To get a better understanding of the role of human resource constraints (HRC) in cost effectiveness we will first describe the decision rules of cost effectiveness analyses and relate those to a simple model describing an optimization problem in which there is only a constraint on the total health care budget. Within this model, an economic definition of human resource constraints is then developed. Based on this definition we will show the consequences of HRC on the estimation of the ICER and the decision rules of cost effectiveness. Finally, we will end this chapter by presenting some stylized examples which illustrate these consequences.

#### 2.1 Human resource constraints in the context of economic evaluation

#### 2.1.1 Cost effectiveness analyses with only one constraint: the health care budget

If the health care budget is set exogenously (and thus fixed) and the goal is to maximize health all opportunity costs deemed relevant for the decision problem fall within the health care sector. According to the decision rules within a health care perspective, an intervention should be adopted if the present value of health gained due to implementing an intervention outweigh the present value of health foregone (the health benefits of the displaced activities):

$$\Delta h > \frac{\Delta c}{k} \tag{1}$$

Where  $\Delta h$  and  $\Delta c$  denotes health gained/incremental costs due to some intervention and k the threshold. Here, the threshold represents the ICER of the displaced health care programs (i.e., in theory the least cost-effective program that was still funded). Equation (1) simply states that a new intervention should be adopted if the health benefits of that intervention are larger than the health benefits foregone due to disinvestment in the intervention that will be displaced. Equation (1) can be rearranged to obtain the decision rule that costs per QALY need to be lower than the threshold in order to be adopted:

$$\frac{\Delta c}{\Delta h} < k \tag{2}$$

More formally, equations (1) and (2) can be derived from an optimization problem in which the health care budget is fixed and the goal is to assess the optimal mix of different interventions which all result in health gains at a certain cost. A simple model would be to consider two different patient populations and one health care budget (denoted *B*). Let *i* and *j* indicate the interventions for these two patient groups. Total health *h* and total health care spending *c* is a function of these interventions. To solve this optimization problem we will define a Lagrangian function *L*:

$$Max L = h(i,j) + \lambda[B - c(i,j)]$$
(3)

First order conditions of this optimization problem are:

$\frac{\partial L}{\partial i} = 0 \rightarrow \frac{\partial h}{\partial i} = \lambda \frac{\partial C}{\partial i}$	(4)
$\frac{\partial L}{\partial j} = 0 \rightarrow \frac{\partial h}{\partial j} = \lambda \frac{\partial C}{\partial j}$	(4)'
$\frac{\partial L}{\partial \lambda} = 0  \rightarrow B = c(i,j)$	(4)''

Rearranging (4) and (4)' shows that at the optimum the marginal returns (in terms of health) to spending in one patient group should equal the marginal return of health care spending of the other patient group:

$$\frac{\frac{\partial h}{\partial i}}{\frac{\partial c}{\partial i}} = \frac{\frac{\partial h}{\partial j}}{\frac{\partial c}{\partial j}}$$
(5)

More importantly, (4) is similar to equation (1) and can be rearranged to obtain the ICER for spending on interventions *i* and *j* if we make use of the fact that  $\lambda$  can be interpreted the amount of QALYs that can be obtained by increasing the budget with one unit. This shadow price equals the inverse of the ICER of the displaced activities within the health care budget  $(k = 1/\lambda)$  which allows to state the following:

$$\frac{\frac{\partial C}{\partial i}}{\frac{\partial h}{\partial i}} = k \tag{6}$$

$$\frac{\frac{\partial C}{\partial j}}{\frac{\partial h}{\partial j}} = k \tag{6}'$$

#### 2.1.2 Defining human resource constraints

To better understand the nature of human resource constraints it is insightful to divide total health care spending into spending on human resources (salaries on nurses and doctors) and spending on other resources within the health care sector (e.g. medicines, equipment).

Furthermore, let us decompose the total health care budget into a budget indicating spending on labour (denoted  $B_l$ ) and a budget indicating spending on non-labour (denoted  $B_o$ ):  $B = B_l + B_o$ . Also, costs of each health care program can be broken down by costs related to labour ( $c_l$ ) and other spending ( $c_o$ ) :  $c(i,j) = c_l(i,j) + c_o(i,j)$ . The Lagrangian function L can now be written as:

$$Max \ L = h(i,j) + \lambda_{l}[B_{l} - C_{l}(i,j)] + \lambda_{o}[B_{o} - C_{o}(i,j)]$$
(7)

First order condition with respect to interventions for patient group *i* is now:

$$\frac{\partial L}{\partial i} = 0 \rightarrow \frac{\partial h}{\partial i} = \lambda_l \frac{\partial C_l}{\partial i} + \lambda_o \frac{\partial C_o}{\partial i}$$
(8)

The big difference with equation (4) is that there are two lambas:  $\lambda_l$  and  $\lambda_o$ . These both can be interpreted as shadow prices: the shadow price of labour and the shadow price of nonlabour. If the total health care budget can be allocated without restrictions (that is *B* can be allocated to labour in any way as long as  $B = B_l + B_o$ ) these shadow prices should be equal in the optimum and the marginal benefits (in term of health) of increasing health care spending on labour should equal the marginal benefits of other health care spending. Thus, in the optimum  $\lambda_l = \lambda_o$  in which case it will also equal  $\lambda$  which allows us to state the following:

$$\frac{\partial h}{\partial i} = \lambda_l \frac{\partial C_l}{\partial i} + \lambda_o \frac{\partial C_o}{\partial i} = \lambda_l \left[ \frac{\partial C_l}{\partial i} + \frac{\partial C_o}{\partial i} \right] = \lambda \frac{\partial C}{\partial i} = \frac{\partial C}{\partial i} / k$$
(9)

In terms of ICERs this equals:

$$\frac{\frac{\partial c_l}{\partial i} + \frac{\lambda_0 \partial c_0}{\partial i}}{\frac{\partial h}{\partial i}} = \frac{1}{\lambda_l} \to \frac{\frac{\partial c_l}{\partial i} + \frac{\partial c_0}{\partial i}}{\frac{\partial h}{\partial i}} = \frac{1}{\lambda} \to \frac{\frac{\partial c}{\partial i}}{\frac{\partial h}{\partial i}} = k$$
(10)

Given this definition of optimality it is also possible to give a clear definition of human resource constraints. We can speak of HRC if the shadow price of labour spending is higher than the shadow price of other health care spending. In other, words, if one additional dollar/pound/euro on labour yields more health gains than one additional dollar in other health care spending. More formally, one can speak of HRC if:

$$\lambda_l > \lambda_o \to k_l < k_o \tag{11}$$

If  $k_l < k_o$  it would be optimal to reallocate the total health care budget towards more spending on labour. This would reduce  $k_o$  and increase  $k_l$ . However, in practice this might not be possible. A reason for this might be shortage of doctors and/or nurses. This causes that the health care budget cannot be spent efficiently. This has as consequence that possible costeffective interventions that require a lot of labour cannot be implemented forcing the health care budget to be spent on interventions that are less cost-effective but require less labour. Also note that HRC imply that  $k_l < k < k_o$ .

#### 2.2 Implications of HRC for economic evaluation

#### 2.2.1 Estimation issues

From section 2.1 it can be clearly concluded that from an economic perspective a limited and/or poorly-skilled workforce in itself cannot be classified as a constraint. Only if the allocation of the health care budget is suboptimal, in the sense that not enough can be spent on human resources we can speak of HRC in an economic sense. What are the consequences of HRC on the estimation and presentation of the ICER? To what extent does if differ from an economic evaluation without HRC? Even in a setting without HRC (in an economic sense) it might be the case that an intervention that is cost-effective for an individual patient (assuming a skilled workforce) might be less cost effective if this intervention is scaled to a population level (which might be the result of a less skilled workforce or issues related to implementation). There is guite some literature in the area of health economics on these issues (Fenwick et al. 2008; Hoomans and Severens, 2014). Key insights from this literature are that if additional costs are needed to more fully implement an intervention, these costs need to be included in the analyses. Furthermore, if there are decreasing or increasing returns to scale when delivering a health care technology, various levels of implementation could be presented as separate mutually exclusive scenarios to be judged incrementally. Summarizing, irrespective whether there are HRC in an economic sense or not, a proper economic evaluation should reflect the fact that implementation in practice might not automatically imply that the technology can be delivered to the entire patient population without any costs given shortages or lack of skills in the workforce. Ignorance of such issues is always wrong to begin with even in the absence of HRC. In this sense, the estimation of the ICER is in itself not influenced by HRC: a good ICER should incorporate local circumstances. As part of the ICER, estimating the costs in terms of wages, time etc. in the presence of HRC is not different than not in the presence of HRC.

The differences between HRC and no HRC become apparent if we look at the opportunity costs of implementing a new intervention. It is the estimate of opportunity costs that is different in the presence of HRC. In other words, the value of what is displaced is different

when there are HRC. If there are no HRC, the value of what is displaced should be equal in different sectors of the health care system. However, in case there are HRC the value of displacing labour is higher than elsewhere in the health care sector.<sup>1</sup> This has important consequences for the presentation and interpretation of CEA studies. If there are no HRC but implementation is not 100% the opportunity costs of additional investments to increase implementation are the same as for any other technology. However, HRC imply the opportunity costs of more labour intensive interventions to be higher than those of less labour intensive interventions. Although these differences might be difficult to quantify empirically, this can itself not be an excuse to ignore them.

#### 2.2.2 Decision rules

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Section 2.1 shows that human resource constraints can be defined as meaning that the marginal benefits of labour investments are higher than those of other health care spending. This has clear implications for the decision rules of cost effectiveness analyses. Most importantly, previous section shows that shadow prices (and thus thresholds) for labour and other spending differ. Using similar notation as in the previous section we could rewrite the decision rules (1) and (2) to the following decision rules if there are human resource constraints:

$$\Delta h > \frac{\Delta c_l}{k_l} + \frac{\Delta c_o}{k_0} \tag{12}$$

$$\frac{\frac{\lambda c_0}{k_l} \Delta c_l + \Delta c_o}{\Delta h} < k_0 \tag{13}$$

Equations (12) and (13) make clear that in theory we should use two thresholds rather than one.<sup>2</sup> Either the costs of labour are given a heavier weight in the ICER or the calculation of health benefits foregone should be broken down into two parts. Note that equation (12) is more intuitive to interpret than equation (13) and can be generalised to more constraints. Crucial is that we need to know which costs fall on which constraint as opportunity costs differ between constraints. Ideally,  $k_o$  and  $k_l$  could be estimated by setting up a mathematical programming model which requires an enormous amount of data. However, we might develop some rules of thumb that may guide the HTA practitioner and policy makers in the absence of a mathematical programming model by using a simple stylized example.

<sup>&</sup>lt;sup>1</sup> Note that our definition of HRC is distinct from that of allocative inefficiency. Conditional on the human resource available it may well be the case that the production of health is efficient.

<sup>&</sup>lt;sup>2</sup> Equations (12) and (13) are similar to the decision rules derived by Claxton et al. (Claxton et al. 2010) in case the consumption value of health is higher than the cost-effectiveness threshold.

#### 2.3 Stylized example

To illustrate the impact of HRC on decision rules and show what can go wrong if the default decision rules are applied when there are HRC consider the following interventions:

- Intervention X1 results in a health gain of 1 QALY per patient and requires 100 dollar of which 80 dollar consists on spending on labour;
- Intervention X2 results in a health gain of 1 QALY per patient and requires 200 dollar of which 50 dollar consists on spending on labour.

Intervention	QALYs gained per person	Total cost	Labour cost
X1	1	100	80
X2	1	200	50

Table 2.1: input values for stylized example

Assume that these interventions are for different patient groups (and thus independent). Besides, there is no shortage of patients to treat and the workforce can perform all said interventions. If we have a health care budget of 2000 dollar we would simply invest all in X1 which results in 20 patients being treated and total health gains of 20 QALYs. The threshold in this case would be 100 dollar per QALY and 1600 dollar would be spent on labour. However, suppose there is a shortage of doctors and only 1000 dollar can be spent on labour. What would then be the optimal allocation of resources? If we solve this optimization problem by filling in the values for our example into equation (7) 9.1 patients would get intervention X1 and 5.5 patients would get intervention X2 resulting in total health gains of 14.6 QALYs. Relaxing the HRC could thus potentially result in a gain of 5.4 QALYs. However, note that relaxation of the HRC in itself needs investments. The thresholds  $k_l$  and  $k_o$  can now also be calculated by simply increasing the budgets for labour and other health care expenses. Results reveal that  $k_l$  equals 86 dollar per QALY and  $k_0$  equals 367 dollar per QALY. Note that increasing the labour budget with 100 dollars will result in a health gain more than 1 QALY because X1 increases by more than 1 patient because of disinvestment in X2 (substitution effects). Vice versa, increasing the health care budget without relaxing the HRC with 200 dollars (the costs of X2) will result in less than 1 QALY gain because of substitution from X1 to X2.

Now let us turn to the interesting question how we should evaluate new interventions given that we have a HRC as described in the above example (1000 dollar budget for labour). Let us introduce two new interventions:

- Intervention X3 results in a health gain of 1 QALY per patient and requires 250 dollar of which only 10 dollar consists on spending on labour;
- Intervention X4 results in a health gain of 1 QALY per patient and requires 90 dollar of which 100% dollar consists on spending on labour.

Intervention	QALYs gained per person	Total cost	Labour cost
X1	1	100	80
X2	1	200	50
X2	1	250	10
X4	1	90	90

If we would apply the default decision rules as in equations (1) and (2) we would adopt X4 because of the low ICER. This would result in health losses because of the shortage of labour. However, if we solve now the optimization problem taking into account the HRC results indicate that X3 will be adopted and X4 not. More specifically, there will be disinvestment in X2 so that in the optimum 12.1 patients receive X1 and 3.2 patients receive X3 resulting in a total health gain of 15.3 QALYs. Although X3 is not that cost-effective it requires almost no labour so adopting this intervention creates a big substitution towards more cost-effective it is very labour intensive. In other words, for interventions that are more labour intensive  $k_l$  is more relevant while for interventions that are not labour intensive  $k_o$  is more relevant (see equations (12) and (13)).

Please note that in this chapter we made a distinction between expenses on labour and all other expenses but that the principles apply much more generally. For instance, we could have more than one type of labour expenses (e.g. spending on nurses and spending on doctors) which is relevant for cost analyses of task shifting.

# 3. Literature review

#### 3.1 Aim and approach

In the previous chapter we gave a definition of HRC in the context of cost effectiveness analysis. Based on that definition we made a distinction between the consequences of HRC on the estimation of the ICER and the threshold. We argued that it is primarily the latter which complicates the use of cost effectiveness analysis. In this chapter we explore and discuss how published studies in the area of cost effectiveness address HRC. Questions we hope to answer with the literature review are the following:

- Which type of studies talk about HRC?
- How do studies define HRC and address HRC in the estimation?
- In what aspects can current studies improve?

To answers these questions we conducted a literature review. We searched the literature for economic evaluations of healthcare technologies and mention/acknowledge human resource constraints. The searching theme consisted of 3 key components: economic evaluations in terms of cost-effectiveness analysis (CEA) or cost-benefit analysis (CBA), human resources (e.g. manpower, workforce, doctor, nurse, and healthcare personnel), and constraints (e.g. shortage, constraint, capacity and additional/extra). We used the following 7 databases: Embase, Web-of-science, Medline, CINAHL, Psycinfo, Cochrane, Google scholar. In addition to searching these databases we also consulted experts: 145 electronic mails were sent to 131 ISPOR chairs and members, 8 corresponding authors of related articles and 6 experts in organizations involved in economic evaluation in LMIC (e.g. IHPP, Radboud University, WHO).

#### 3.2 Findings

#### 3.2.1 Which type of studies talk about HRC?

We found 1,132 articles from searching the electronic databases (note that a quick search on just economic evaluation yields about 100,000 hits). After deduplication, there are 863 articles left. Following up with expert consultation, we received 31 replies and 21 additional articles were suggested. Of these 884 articles in total many articles were excluded, such as articles not dealing with health care in any way, editorials or opinion articles and systematic review articles. As a result, only 185 articles remained to be screened. Figure 3.1 displays the results schematically.

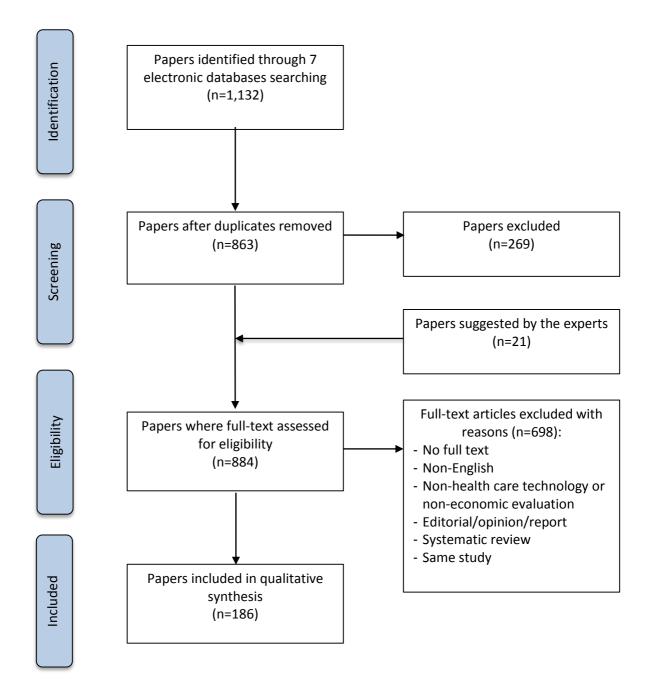


Figure 3.1: process of literature review

We screened title and abstract of the remaining articles 186 and then read the full-text of them if some constraint-related words were found in the abstract. Table 3.1 summarises all the 186 articles that were found. Of those 186 articles, 106 articles used primary data while the other 80 articles relied exclusively on secondary data and modelling. About 20% of the articles were conducted in the setting of low-middle income countries (LMICs). Most studies focused on the area of disease diagnosis and treatment.

Category	Primary data use (106)	Modelling use (80)
LMIC (N=40)	29	11
Primary prevention* (N=74)	39	35
Disease diagnosis and treatment (N=108)	64	44
Rehabilitation (N=4)	3	1

Table 3.1 summary statistics of studies found in the review (N=186)

\*Including screening and vaccination

#### 3.2.2 How do studies define and address HRC?

In none of the papers described in table 3.1, HRC were defined explicitly. Mostly, HRC were mentioned in the paper to give a better description of local circumstances. Consequently, possible consequences of HRC for the estimation of opportunity costs and decision rules were also never mentioned. Some papers, however, did take into account HRC when estimating the expected costs and benefits of particular interventions. To answer the question how studies address HRC in the estimation of the costs and benefits we made a distinction between the following three categories:

- 'Ignoring': studies in which HRC are mentioned but not taken into account in any way when estimating the ICER;
- 'Incorporating': studies in which HRC are recognized and addressed when estimating the ICER;
- 'Relaxing': studies in which HRC are explicitly relaxed in any way, such as investments in training staff.

Table 3.2 displays the categorization of the studies in these three categories stratified by whether they used primary data or relied exclusively on secondary data and modelling.

Table 3.2: classification of studies depending on how they addressed HRC in the estimation of the ICER (N=186)

Category	Primary data use (105)	Modelling use (80)	
Ignoring (166)	91	75	
Incorporating (4)	1	3	
Relaxing (16)	14	2	

From Table 3.2 we can observe that most studies that mention HRC do not take this into account when estimating the ICER. Only a few studies incorporate or relax the constraints. Of

the articles in the relaxing category, studies in the area of task-shifting were most frequently encountered. To get a flavour of the categories 'ignoring', 'incorporating and 'relaxing' the text boxes on the following pages describe the main features of some selected studies in the different categories. For some studies we also identify some weaknesses in terms of addressing HRC and give suggestions on how to overcome them.

#### Textbox 1: example of ignoring HRC in a study using primary data

Primary data use: Cost-effectiveness of eye care services in Zambia', by Griffiths, et al., 2014.

The article presents an economic evaluation (from a societal perspective) comparing two eye care services in Zambia: cataract surgery and refractive error correction, compared to the situation before using these services. In this prospective study 170 cataract and 113 refractive error/presbyopia patients were included. Costs were determined from patient interviews and micro-costing at the three health facilities. After six months of follow-up, data were available from 77 and 41 patients who had received cataract surgery and spectacles, respectively. Utility values were estimated using the EQ5D and costs were estimated by adding patient specific and facility overhead costs to all patients whether they were treated or not. Costs that were allocated to those who attended the facilities but did not receive the expected care were excluded in the calculations. The cost and QOL data informed a decision analytic model for estimating the cost-effectiveness of cataract surgery and RE/ presbyopia correction.

Results show that utility values significantly improved across the patient sample after cataract surgery and acquiring spectacles. Incremental costs per Quality Adjusted Life Years gained were US\$ 259 for cataract surgery and US\$ 375 for refractive error correction. Although these eye interventions could be proven highly cost-effective in Zambia, when interpreting their results, the authors acknowledged that severe health care system constraints including HRC are likely to hinder scaling-up the programs.

Given the crisis in the workforce shortage (HRC), authors reported that only 45% of cataract patients and 36% of refractive error patients received the expected care. As the calculations were made on the patient individual level, the constraints do not influence the estimates of health effects in this paper, unless the disease progresses and a diminishing utility value could have been the case. However, known costs, which were allocated to those who attended the facilities but did not receive the expected care, were excluded in the calculations. By definition, this leads to an underestimation of ICERs.

#### Textbox 2: example of incorporating HRC in a modelling study

Modelling use: 'Cost-effectiveness of cognitive behavioural therapy (CBT) and selective serotonin reuptake inhibitors (SSRI) for major depression (MDD) in children and adolescents', by Haby et al., 2004.

The article presents a model based economic evaluation of psychiatric treatments for major depression (cognitive behavioural therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs)), compared to the current practice in Australia. A decision tree reflecting the clinical pathway analysis was based upon a time horizontal of one year and analysis were based on a health sector perspective. Data were tracked from children aged 6-17 years with a new episode of MDD who were seeking care and would have received the usual care (n=10,952). Effect size and resource usage was estimated from other literature and expert advice, and unit costs were adopted from Australian Department of Health and Aging. The study addressed human resource constraints (HRC) in terms of the limited availability of skilled clinicians and motivation of clinicians and patients. For this purpose these constraints were included in a model parameter called 'adherence'. The adherence parameter was varied between 50% and 85% for CBT and 50% and 76% for SSRI. They were then used in the uncertainty analysis after the usual calculations of cost-effectiveness.

Compared to current practice, CBT by public psychologists is the most cost-effective intervention for MDD in children and adolescents at A\$ 9000 per DALY saved. Taking HRC into account (by varying the adherence parameter in Monte Carlo simulations) the estimates varied from A\$ 3900 to A\$ 24,000.

This study clearly shows that when HRC are explicitly incorporated in cost-effectiveness modelling, the estimates of ICER vary from not taking these constraints into account. However, as the authors used only one parameter in the model to incorporate not only HRC but also various other limiting factors, it impossible to disentangle the impact of HRC from these other factors.

Primary data use: 'Cost Effectiveness of Community Based Strategies for Blood Pressure Control in a Low income Developing Country: Findings from A Cluster Randomized Factorial Controlled Trial', by Jafar et al., 2011.

This article presents an economic evaluation of community based strategies for blood pressure control in Pakistan. Twelve communities of about 250 households from low-middle income area in Karachi were randomly selected by multistage cluster sampling technique. 1341 newly diagnosed and known hypertensive subjects aged 40 and above in these communities were enrolled and masked to their randomization status. The 12 selected communities were equally allocated to four groups of scenario consisting of three groups. These groups reflected different strategies for relaxing the human resource constraints: 1) combined home health education (HHE) with trained GPs 2) only HHE and 3) only trained GPs, and one group of the current usual care which was implicitly assumed that there are the constraints. Cumulative costs of intervention including personnel, equipment, and training material and supplies for development of curricula, and transport and other operational expenses, were estimated over 2 years and compared to the baseline from the perspective of the policymaker. Blood pressure before and 2 year after the intervention was recorded and used as health effects. Calculations of cost-effectiveness were then made for each scenario and compared.

The results show that the combination of HHE and trained GPs with an ICER of \$23 per mmHg reduction is more cost-effective than the usual care and other single intervention-strategies. Based on the results the authors suggest that it is worth to invest in human resources. Furthermore, the authors argue that the results can also be generalised to other countries with a similar healthcare infrastructure like Indo-China countries.

In the article, no explicit mention is made about the extent to which human resources constraints already exist or might constrain the full implementation of the intervention.

Modelling use: 'Antiretroviral drugs as a public health intervention for pregnant HIVinfected women in rural South Africa: an issue of cost-effectiveness and capacity', by Wilkinson et al., 1998.

The article presents estimates of cost-effectiveness and capacity requirements for providing antiretroviral drugs to pregnant women in South Africa. It first anticipated possible obstacles to deliver the drug such as lack of staff, poor access to the care and then proposed a solution to relax those constraints, i.e. enhancing capacity, consisting of encouraging early attendance of antenatal care by health promotion and training extra staffs for antiretroviral drugs. Three scenarios of providing the drugs were made based on assumptions including 1) Zidovudine delivered in the existing infrastructure (A) 2) Zidovudine delivered though enhanced infrastructure (B) 3) Short course Zidovudine plus Lamivudine delivered though enhanced infrastructure (C). To estimate the costs a *top-down approach* was used: one lump of money was spent once on investment in enhancing the capacity, with mainly an increase in the number of health workers. These three scenarios were compared their costs and effectiveness with the situation of no intervention in 1997. Intervention costs were estimated from the perspective of the health system. Effectiveness in each scenario was also made based on assumptions.

Results indicate that scenarios with enhanced infrastructure as a way of relaxing the constraints with ICERs of US\$ 5591 and US\$ 2492 for scenario B and C, retrospectively, are more cost-effective than scenario A. In the article, however, scenarios with relaxing the constraints (scenarios B and C) were only compared to the situation in which constraints were not relaxed (scenario A) and not compared incrementally (C compared to B). Such an incremental comparison would reveal that scenario B is dominated by scenario C which can be informative for decision making.

#### **3.3** How can we improve current studies?

The textboxes in the previous section have given already us ideas how to improve on current studies. First of all, most studies we identified in our search do not provide an explicit definition of HRC (not in an economic sense nor in any other sense). Furthermore, although in our opinion, the concept of opportunity costs is particularly relevant in the context of HRC these studies pay no attention to this concept. The relevance of opportunity costs is most easily demonstrated for the cost effectiveness analysis on task shifting. The motivation for investigating the cost effectiveness of task shifting usually is the presence of HRC and the idea that highly skilled/trained labour (which is scarce) can be made more productive if some of their tasks can be shifted to other less scare labour forces (often also less skilled). Here, there is an explicit recognition that the opportunity costs might differ strongly between the different types of workers. However, in the cost effectiveness analyses presented these differences are ignored. In the studies we looked at a task shifting intervention was considered to be cost effective if the ICER of performing a particular intervention by the less skilled was lower than that of the more skilled worker. However, in case there are HRC, this is not relevant as opportunity costs in terms of health foregone are higher for the skilled workers. When relaxing HRC, it is important to realize where resources are being drawn from and what the value is of what is being displaced. However, none of the studies discuss the value of what might potentially be displaced when tasks are shifted between different types of health workers (for instances nurses vs doctors).

Secondly, there is also much room for improvement in the estimation of the ICER in the presence of HRC. We saw that many studies simply did not do a very good job in adapting to local circumstances. Often, it is simply assumed that a technology will be implemented under perfect circumstances for the entire population and issues related to the costs of implementation and decreasing/increasing returns are not addressed in the analyses. These issues could be addressed in the standard cost effectiveness framework in scenario analyses which are compared incrementally. The paper by Wilkinson was one of the few studies that actually estimated the costs and benefits of relaxing HRC but failed to compare the scaling up of interventions incrementally.

#### 3.4 A worked out example based on the literature

To illustrate how to incorporate HRC instead of ignoring HRC in the estimate of costeffectiveness we will use the study by Griffiths et al. (2014) as an example (see textbox 1). In this study, the cost effectiveness of two eye care services in Zambia were estimated: cataract surgery and refractive error correction. However, in the estimation of the ICER local circumstances were not completely incorporated as the ICER estimates excluded some cost that were the consequence of a suboptimal implementation due to the shortages in the workforce. Therefore, we recalculated the ICERs using the information regarding costs and health effects as presented by the authors. As such, in contrast to the original calculations, the total overhead costs are reallocated to only those patients who received the care to obtain the actual costs per actually treated patient, and of course QALYs gained remain unchanged. The comparison between the adapted estimates of ICER and the ones ignoring HRC is presented in the Table 3.3 below. The adapted costs per patient are considerably higher compared to the original estimates: \$132.90 compared to \$92.00 for cataract surgery and \$120.05 versus \$72 for refractive error correction. The adapted cost estimates lead to a higher cost-effectiveness ratio: changing from \$259.15 to \$374.36 per QALY gained for cataract surgery and from \$375.00 to \$625.28 per QALY gained for refractive error correction.

	Cataract surgery (Sx)			Refractive error correction (Cx)		
	Without Sx	With Sx	Incremental	Without Cx	With Cx	Incremental
Ignoring HRC						
Cost (2010)	0.00	92.00	92.00	0.00	72.00	72.00
QALYs	7.52	7.87	0.36	3.66	3.85	0.19
ICER			259.15			3.75
Incorporating HRC						
Cost (2010)	0.00	132.90	132.90	0.00	120.05	
QALYs	7.52	7.87	0.36	3.66	3.85	
ICER			374.36			625.28

Table 3.3: recalculation of ICERs in the' Cost-effectiveness of eye care services in Zambia' study by Griffiths, et al., 2014.

In the absence of HRC the decision rules of cost effectiveness would imply that first all patients who need cataract surgery would be treated before any patients who refractive error correction are to be treated. In the Griffiths study 77 patients received the cataract surgery and 41 patients a refractive error correction. More importantly, almost 100 patients who needed cataract surgery did not receive cataract surgery. One of the reasons mentioned in the study is a shortage of workforce of delivering cataract surgery implying HRC.

To explore the impact of HRC for optimal decisions in the example of Griffith, we first estimated total costs and total labour costs for each of the two interventions based on the data presented in the study. Although the information presented did not allow a precise estimation of labour cost per patient for the two interventions we made a rough estimate of \$20 per patient for cataract surgery and \$10 per patient for the refractive error correction. Based on the number of patients the total budget spent on these two interventions is \$15,153.- of which \$1,950.- on labour and total QALYs gained equal 35.5. However, although cataract surgery is more cost-effective than refractive error correction it is also more labour intensive (it requires more labour costs per QALY gained). Given that cataract surgery is more cost effective and that not all patients who need cataract surgery are treated because of HRC, we then assumed that HRC caused that not more than \$1950.- can be spend on labour. To quantify the impact of HRC we estimated how many QALYs would be gained if the total budget spend (\$15,153.-) could be spend freely (ignoring the labour budget constraint of \$1950.-). In that situation all the budget would be spend on cataract surgery (treating 114 patients) resulting in 41.05 QALYs gained. HRC in this example result in a loss of almost 6 QALYs (more than 10% lower health gains). We estimated  $k_l$  and  $k_o$  by filling in values for equation (7) and making using of the fact that  $k_l = 1/\lambda_l$  and  $k_o = 1/\lambda_o$ :

$$Max L = 0.36i + 0.19j + \lambda_{l} [1950 - 20i - 10j] + \lambda_{o} [13203.3 - 112.9i - 110j]$$
(7)'

Here *i* denotes cataract surgery and *j* refractive error correction. By solving (7)'  $k_l$  was estimated to equal \$59 per QALY gained and  $k_o$  \$5355 per QALY gained.

# 4. Conclusions and recommendations

#### 4.1 Conclusions

In this report we discussed human resource constraints (HRC) in the context of health economic evaluations. First, we gave a definition of HRC in terms of economic efficiency derived from a theoretical model describing the optimal allocation of the health care budget. HRC imply (or can be defined as) that the health gains of increasing the labour budget by one unit are higher than that of increasing other budgets on health care spending. This definition is different from a more 'lay view' definition of HRC which usually refers to issues relating to the implementation of new technologies. The crucial difference is that in our definition HRC imply that the opportunity costs of more labour intensive technologies are higher than less labour intensive technologies. If there are no HRC, in theory opportunity costs should be equal in different health care sectors and the marginal benefits of an additional dollar spending on labour should be the same as the marginal benefits of spending an additional dollar spending on non-labour (e.g. medication or technical facilities). This also implies that the main difference when conducting cost effectiveness in the presence of HRC (compared to no HRC) lies in the estimation of opportunity costs. If there are HRC, it is not only the estimation of the ICER that is influenced but also the estimate of the value of what is displaced. In other words, the decision rules are impacted. In the presence of HRC, it is misleading to look at the ICER of the least cost-effective program still funded. In the presence of HRC labour intensive interventions need to be compared to a lower threshold than interventions that require less labour. Interventions that do not require much scarce labour could have an ICER that is higher than the ICER of the least cost-effective program still funded.

From the literature review we found that no study explicitly defined HRC. Most often, studies mention human resources constraints in a more colloquial manner. As a results, as far as we could identify, not a single study acknowledges that opportunity costs might differ in the presence of HRC. Interestingly, a more conceptual paper in the area of human resources explicitly stresses the relevance of opportunity costs when evaluating task-shifting interventions (Fulton et al., 2011):

# 'Additionally, the opportunity cost of task shifting needs be incorporated into an evaluation, because a cadre that has shifted tasks will no longer be able to perform its original tasks.'

Furthermore, the literature review reveals that also the majority of studies ignore HRC when estimating the costs and benefits of interventions resulting in biased estimates of cost

effectiveness. Studies that explicitly were aimed at relaxing constraints were mainly in the area of task shifting.

#### 4.2 Recommendations

The goal of this study was to develop guidance on how to incorporate, present and reflect upon HRC in cost effectiveness analyses. We argued that HRC constraints become most relevant when researchers start to address opportunity costs. However, also when researchers estimate costs and benefits of technologies, these might be influenced by HRC. Both of these mechanisms have clear implications on how to incorporate, present and reflect upon HRC in cost effectiveness analyses. Based on our theoretical model and findings of the literature, we have the following recommendations:

- 1. Estimates of costs and benefits of health care technologies should incorporate HRC. Currently, many cost effectiveness studies ignore HRC when estimating costs and benefits of health care technologies. While this offers relevant information of the efficiency of new technologies under perfect circumstances (which might be achievable in the long run), it does not give insights into how these technologies might work out in practice. Furthermore, as investments are needed to relax constraints in order to reach perfect circumstances, it might not always be cost-effective to operate technologies under perfect circumstances (Fenwick et al. 2008; Hoomans and Severens, 2014). We therefore recommend that estimates presented in economic evaluations should always reflect HRC, next to presenting the efficiency of a technology ignoring HRC. Conventional techniques of estimating costs and benefits of health care technologies can be applied to accomplish this aim.
- <u>Researchers should focus less on estimating and presenting ICERs and present more disaggregated results.</u>

The conventional ICERs presented in economic evaluations are most useful if the only relevant constraint is the budget that can be spend on health care. However, in the presence of HRC (or other constraints) these ICERs become less informative. In order for economic evaluations to be useful, less focus should be placed on only estimating and presenting the ICER. Rather, it is better to present results in a manner that aligns with relevant constraints. For instance, in the context of HRC it is important that results of economic evaluations need to be presented so that decision makers can see how much labour costs are required to gain QALYs. Presenting results specified regarding type of constraint facilitates the calculation of 'health gains' and 'health foregone' of different policy options.

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#### 3. In the presence of HRC opportunity costs need to be discussed explicitly

A distinctive feature of HRC is that they imply that the opportunity costs of more labour intensive health care interventions are higher than those less labour intensive interventions. In the applied cost effectiveness literature, this issue is not discussed at all. Even in the absence of good empirical estimates of opportunity costs, the issue of how HRC affect opportunity costs needs to be discussed properly in applied cost effectiveness analysis. Crucial is that opportunity costs are constraint specific and in the case of HRC, opportunity costs are higher the more labour intensive a technology is.

4. <u>Future research should focus on better empirical estimates of opportunity costs</u> reflecting HRC.

In the presence of HRC, opportunity costs differ depending on the amount of labour that is required for the new technologies. Ideally, estimates of opportunity costs should reflect this. To estimate opportunity costs reflecting HRC additional research is needed.

- 5. In the absence of good empirical estimates of opportunity cost reflecting HRC simple models and rules of thumb can be used to improve recommendations. Even in the absence of estimates of opportunity costs reflecting HRC ignoring HRC when making recommendations is not the way forward. Rather, we advise to make use of rules of thumb. Here we present some simple rules of thumb that could be of value when making recommendations based on economic evaluation conducted in the presence of HRC:
  - New technologies that are cost-effective compared to currently funded programs but require lots of skilled labour should not automatically be funded;
  - b. New technologies that are not cost-effective compared to currently funded programs but require not much skilled labour can be attractive!

All recommendations imply that more is to be expected from researchers in individual cost effectiveness studies. While all recommendations are relevant for researchers conducting economic evaluations especially recommendation 5 is also relevant for decision makers. Most important is that decision makers should be presented with data and advice on ways to interpret them by researchers so they may make their own decisions. Over time, researchers and decision makers will be able to examine a growing bank of other, more general studies and use these to interpret opportunity costs and CEA results in the presence of HRC. While there is no need to use mathematical programming for every CEA on a new drug, mathematical programming probably remains the way to go when multiple constraints need to be considered for a large set of interventions as decision rules quickly become complex.

# 4.3 Closing remarks

Although our starting point was that of incremental economic evaluations targeted at decision makers who might not have the discretion to relax HRC, HRC itself signal that the health system needs strengthening in terms of human resources. An important question then is whether investments in health systems need priority compared to investments into specific health care technologies (Morton et al. 2015). Although this question is beyond the scope of this report, we do think it is important to emphasize the importance of this question. Answering this question might guide more long term strategic planning of health care systems and the health care workforce.

# References

Adang, Eddy MM. "Economic Evaluation of Innovative Technologies in Health Care Should Include a Short-Run Perspective." The European Journal of Health Economics 9, no. 4 (2008): 381-84.

Claxton, K., Walker, S., Palmer, S., Sculpher, M. 2010. Appropriate perspectives for health care decisions Appropriate Perspectives for Health Care Decisions. CHE Research Paper 54

Drummond, Michael F., Mark J. Sculpher, George W. Torrance, Bernie J. O'Brien, and Greg L. Stoddart. Methods for the Economic Evaluation of Health Care Programmes. 3 ed: Oxford University Press, 2005.

Epstein, David M, Zaid Chalabi, Karl Claxton, and Mark Sculpher. "Efficiency, Equity, and Budgetary Policies Informing Decisions Using Mathematical Programming." Medical Decision Making 27, no. 2 (2007): 128-37.

Feenstra, Talitha L, Pieter M van Baal, Monique O Jacobs-van der Bruggen, Rudolf T Hoogenveen, Geert-Jan Kommer, and Caroline A Baan. "Targeted Versus Universal Prevention. A Resource Allocation Model to Prioritize Cardiovascular Prevention." Cost Eff Resour Alloc 9, no. 1 (2011): 14-19.

Fenwick, Elisabeth, Karl Claxton, and Mark Sculpher. "The Value of Implementation and the Value of Information: Combined and Uneven Development." Medical Decision Making 28, no. 1 (2008): 21-32.

Fulton, Brent D, Richard M Scheffler, Susan P Sparkes, Erica Yoonkyung Auh, Marko Vujicic, and Agnes Soucat. "Health Workforce Skill Mix and Task Shifting in Low Income Countries: A Review of Recent Evidence." Hum Resour Health 9, no. 1 (2011): 1.

Griffiths, Ulla K, Fiammetta M Bozzani, Adrian Gheorghe, Lawrence Mwenge, and Clare Gilbert. "Cost-Effectiveness of Eye Care Services in Zambia." Cost Effectiveness and Resource Allocation 12, no. 1 (2014): 6.

Haby, Michelle M, Bruce Tonge, Lyn Littlefield, Rob Carter, and Theo Vos. "Cost-Effectiveness of Cognitive Behavioural Therapy and Selective Serotonin Reuptake Inhibitors for Major Depression in Children and Adolescents." Australian and New Zealand Journal of Psychiatry 38, no. 8 (2004): 579-91.

Hoomans, Ties, and J Severens. "Economic Evaluation of Implementation Strategies in Health Care." Implement Sci 9 (2014): 168.

Jafar, Tazeen H, Muhammad Islam, Rasool Bux, Neil Poulter, Juanita Hatcher, Nish Chaturvedi, Shah Ebrahim, and Peter Cosgrove. "Cost-Effectiveness of Community-Based Strategies for Blood Pressure Control in a Low-Income Developing Country Findings from a Cluster-Randomized, Factorial-Controlled Trial." Circulation 124, no. 15 (2011): 1615-25.

Karlsson, Gv∂ran, and Magnus Johannesson. "The Decision Rules of Cost-Effectiveness Analysis." Pharmacoeconomics 9, no. 2 (1996): 113-20.

Morton, Alec, Ranjeeta Thomas and Peter C Smith "Decision rules for allocation of finances to Health Systems Strengthening" 2015 *Submitted* 

Murray CJ, Evans DB, Acharya A, Baltussen RM. "Development of WHO guidelines on generalized cost-effectiveness analysis." Health Econ. 2000 Apr;9(3):235-51.

Robinson, Mary, and Peggy Clark. "Forging Solutions to Health Worker Migration." The Lancet 371, no. 9613 (2008): 691-93.

Smith, Peter C., Ranjeeta Thomas, and Katharina Hauck. "Departures from Cost-Effectiveness Recommendations: The Impact of Health System Constraints on Priority Setting." (2014).

Stinnett, Aaron A, and A David Paltiel. "Mathematical Programming for the Efficient Allocation of Health Care Resources." Journal of Health Economics 15, no. 5 (1996): 641-53.

Van de Wetering, Gijs, Willem H Woertman, and Eddy MM Adang. "A Model to Correct for Short, Inefficiencies in Economic Evaluations in Healthcare." Health economics 21, no. 3 (2012): 270-81.

Weinstein, Milton, and Richard Zeckhauser. "Critical Ratios and Efficient Allocation." Journal of Public Economics 2, no. 2 (1973): 147-57.

Wilkinson, David, Katherine Floyd, and Charles F Gilks. "Antiretroviral Drugs as a Public Health Intervention for Pregnant Hiv,Äêinfected Women in Rural South Africa: An Issue of Cost,Äêeffectiveness and Capacity." Aids 12, no. 13 (1998): 1675-82.

World Health Organization. "The World Health Report: 2006: Working Together for Health." (2006).

Wyss, Kaspar. "An Approach to Classifying Human Resources Constraints to Attaining Health-Related Millennium Development Goals." Human Resources for Health 2, no. 11 (2004): 8.