

This is a repository copy of *Economic Analysis for Health Benefits Package Design*.

White Rose Research Online URL for this paper:  
<https://eprints.whiterose.ac.uk/147199/>

Version: Published Version

---

## **Monograph:**

Love-Koh, James [orcid.org/0000-0001-9009-5346](https://orcid.org/0000-0001-9009-5346), Walker, Simon Mark [orcid.org/0000-0002-5750-3691](https://orcid.org/0000-0002-5750-3691), Kataika, Edward et al. (6 more authors) (2019) *Economic Analysis for Health Benefits Package Design*. Discussion Paper. CHE Research Paper . Centre for Health Economics, University of York , York, UK.

---

## **Reuse**

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

## **Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.



Centre For Health Economics



## Economic Analysis for Health Benefits Package Design

James Love-Koh, Simon Walker,  
Edward Kataika, Sibusiso Sibandze,  
Matthias Arnold, Jessica Ochalek,  
Susan Griffin, Paul Revill, Mark Sculpher

**CHE Research Paper 165**

## Economic analysis for health benefits package design

<sup>a</sup>James Love-Koh

<sup>a</sup>Simon Walker

<sup>b</sup>Edward Kataika

<sup>b</sup>Sibusiso Sibandze

<sup>a,c</sup>Matthias Arnold

<sup>a</sup>Jessica Ochalek

<sup>a</sup>Susan Griffin

<sup>a</sup>Paul Revill

<sup>a</sup>Mark Sculpher

<sup>a</sup>Centre for Health Economics, University of York, UK

<sup>b</sup>East, Central and Southern Africa Health Community

<sup>c</sup>Health Economics & Policy Unit, College of Medicine, University of Malawi

June 2019

## **Background to series**

CHE Discussion Papers (DPs) began publication in 1983 as a means of making current research material more widely available to health economists and other potential users. So as to speed up the dissemination process, papers were originally published by CHE and distributed by post to a worldwide readership.

The CHE Research Paper series takes over that function and provides access to current research output via web-based publication, although hard copy will continue to be available (but subject to charge).

## **Acknowledgements**

This work was supported by UK Research and Innovation as part of the Global Challenges Research Fund, grant number MR/P028004/1. No ethical approval was needed. We would also like to thank Karel Haal for his comments on an early draft of this work.

## **Further copies**

Only the latest electronic copy of our reports should be cited. Copies of this paper are freely available to download from the CHE website [www.york.ac.uk/che/publications/](http://www.york.ac.uk/che/publications/). Access to downloaded material is provided on the understanding that it is intended for personal use. Copies of downloaded papers may be distributed to third parties subject to the proviso that the CHE publication source is properly acknowledged and that such distribution is not subject to any payment.

Printed copies are available on request at a charge of £5.00 per copy. Please contact the CHE Publications Office, email [che-pub@york.ac.uk](mailto:che-pub@york.ac.uk), telephone 01904 321405 for further details.

Centre for Health Economics  
Alcuin College  
University of York  
York,  
YO10 5DD, UK

[www.york.ac.uk/che](http://www.york.ac.uk/che)

©James Love-Koh, Simon Walker, Edward Kataika, Sibusiso Sibandze, Matthias Arnold, Jessica Ochalek, Susan Griffin, Paul Revill, Mark Sculpher

## **Abstract**

A health benefits package (HBP) defines the list of publicly provided health services offered by a country's health system. HBPs are seen as an important component toward achieving universal health coverage in low- and middle-income countries. This paper provides an overview of the main considerations that arise when designing and implementing an HBP.

The first set of issues relate to the governance of HBPs. The processes for designing and updating the HBP should be transparent, consistent, stable and involve consultation with appropriate stakeholders. These features can improve public support for the HBP by making decision-makers accountable for choices and the HBP process understandable to citizens.

Economic considerations are also paramount when selecting interventions to include in an HBP. The value of interventions can be judged on multiple criteria that reflect the various objectives of a specific health system. Economic evaluation methods, such as cost-effectiveness analysis (CEA), can be used to generate evidence on outcomes and costs to help decision makers select a package in pursuit of a common health system objective: improving population health. This can yield the list of interventions and the optimal size of the HBP budget that maximise health outcomes.

Economic evaluation methods can also be used to consider how additional health system constraints and objectives can affect decisions around an HBP. These include commitments to principles of equity, limited supply of human resources and equipment, and low levels of implementation.



## 1. Introduction

Universal health coverage is an objective in many low- and middle-income countries (LMICs), having been explicitly set as one of the targets in the United Nations Sustainable Development Goals [1]. Universal health coverage entails the provision of a set of health services to all citizens in a population, regardless of their economic and social circumstances. This presents a prioritisation problem, because resource constraints mean that not all services that offer benefits to patients can feasibly be provided. The set of essential services to be provided universally is commonly referred to as a health benefits package (HBP). The selection of which services to provide (and finance) has been made in different ways and with varying degrees of transparency. Over recent decades, HBPs have been designed for use in countries worldwide, from South America [2] to Central Asia [3]. Within the East, Central and Southern Africa (ECSA) health community region, HBPs have been adopted by Malawi [4], [5], Kenya [6] and Zambia [7]. Three examples are described in Box 1.

Designing an efficient, equitable and sustainable HBP is complex. Some HBPs designed with high aspirations and broad commitments to providing universal health coverage have resulted in financially unaffordable plans that are unable to deliver on their objectives [8], [9]. In response, a process of careful financial planning and an explicit commitment to a clearly and publicly defined set of interventions is recommended [10]. This approach can increase the benefits generated by public healthcare, by allocating resources to those with the greatest capacity to benefit and ensuring that the HBP is financially sustainable.

This briefing paper provides an overview of the main considerations when designing and implementing an HBP. Firstly, the HBP policy cycle is described, a useful framework covering the whole HBP design process. Next, some key concepts on good governance are presented, along with potential political issues that can arise. The remainder of the briefing is dedicated to how methods developed in the economic evaluation of health technologies – namely cost-effectiveness analysis – can be used to develop evidence on what interventions should be included in an HBP.

**Box 1: Examples of health benefits packages in the east, central and southern Africa region****Malawi**

The Malawian HBP, the Essential Health Package (EHP), was first introduced in 2004 and was most recently revised in 2016 as part of the health sector strategic plan for 2017-22 [4]. The EHP was initially funded through a Sector Wide Approach (SWAp), which pooled funding from government and a number of donors into a single account. It is now funded primarily through government funds with targeted assistance from donors and other partners.

Earlier iterations of the EHP resulted in overly ambitious packages that far outstripped available resources; in 2011, the EHP was costed at \$44 per capita despite a budget of \$14.50 [11]. In part, this was motivated by a desire to encourage international donors to increase their financial commitments; however, it also limited the effectiveness of the EHP and created large inequalities in coverage across the population.

The economic analysis supporting the most recent EHP aims to better reflect the costs and opportunity costs (i.e. the health gains achieved through other forms of health spending) of providing each intervention, including the expected limits on population coverage. This work is covered in more detail in Box 2.

**Uganda**

The Ugandan National Minimum Healthcare Package (UNMHCP) was first introduced in the country's health sector strategic plan for 2001/2-2004/5, and has been updated for each subsequent five year cycle. The UNMHCP focuses on providing interventions for those diseases that are responsible for the highest health burden. This yielded twelve 'priority programmes' that were used to identify a range of services to be delivered at each level of health facility; from nutrition monitoring at primary health centres to x-ray examinations at general hospitals.

The estimated costs of delivering the UNMHCP has regularly exceeded the available resources: delivery costs 2008/9 were estimated at \$41.2 per capita, compared to a health budget of \$12.5 [12]. The two most recent strategic plans did not include specific costing exercises for the UNMHCP. Coverage of the services included in the UNMHCP has varied widely, and has been supported by direct grants and support from central government and donor organisations [13].

**Tanzania**

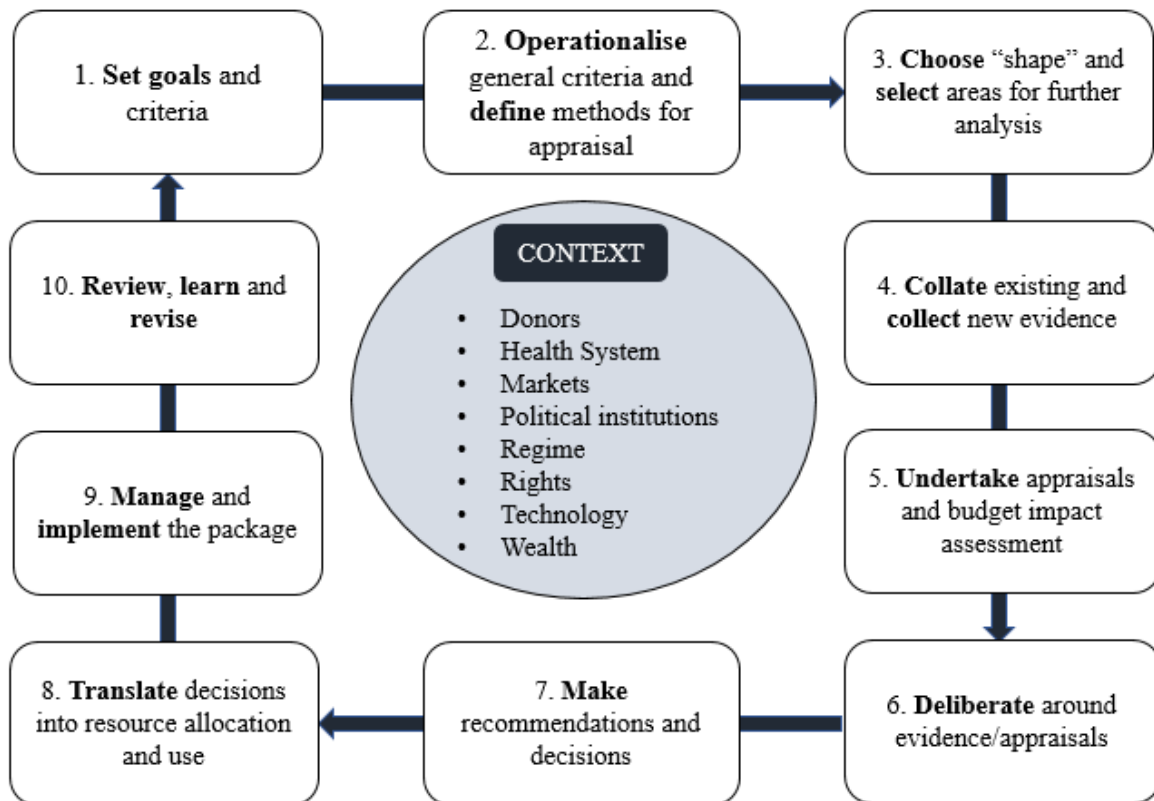
The Tanzanian HBP was introduced in 1996. The most recent package, the National Essential Health Care Intervention Package (NEHCIP-Tz), is being updated as part of the 2015-2020 health sector strategic plan [14] and has replaced the National Package of Essential Health (NPEH). Early efforts focused on establishing evidence generation procedures to help identify disease priorities and cost-effective interventions. Burden of disease was a key criteria for selecting interventions.

By the 2000s, SWAp funding arrangements were in place to finance the NPEH. However, the introduction of vertical, donor financed programs increased the complexity of costing the package [15]. Rather than an explicit set of interventions, the NPEH describes a set of priority conditions (such as malaria or immunisation). However, the most recent strategic plan introduced proposals for a minimum benefit package of services that citizens are legally entitled to access, to be introduced alongside a new national health insurance program. The minimum benefit package is informed by a costing exercise that aligns the included interventions with available health resources, with the hope of ensuring that full implementation is achievable.



## 2. The HBP policy cycle

The construction and maintenance of an HBP is an iterative process, and is dependent on policy choices and the nature of the health system. Glassman and colleagues argue that in order to develop a coherent and sustainable process for setting the HBP, ten core steps need to be fulfilled. Figure 1 illustrates the ‘HBP policy cycle’ that underlines the interdependence of the ten steps [10]. We briefly discuss each in turn.



**Figure 1: Ten core steps in health benefits package design defined by Glassman et al. [16]**

The first step in the design of the HBP is to define the goals and objectives. The goals should be in line with the existing values of the health system and reflect the medical needs of the population. It is important that the objectives are feasible, and sustainable over time.

The objectives should be linked to measurable outcomes that can be robustly appraised (step 2). The use of performance management approaches such as SMART (specific, measurable, achievable, relevant and time-bound) criteria can be beneficial to defining the objectives and the methods of appraisal [17]. In step 3, the ‘shape’ of the HBP is defined. (i.e. the organisational boundaries of the HBP). The shape of the HBP refers to the institutional context in which it operates. An example of the type of decision that determines the shape is whether the HBP is system-wide or is limited to a subset of services (i.e. HIV or TB programmes). This sets the scope within which decision makers then identify priority areas for appraisal.

Steps 4 and 5 are chiefly analytical; they relate to the (i) collection and collation of relevant evidence and (ii) the translation of this evidence into outcomes of interest for decision making, such as population health benefit and budget impact. Evidence collection can be made transparent by utilising the systematic review process, in which the inclusion criteria for evidence are explicit [18]. The evidence should be collated for use in appraisal, by assessing relevance and validity (i.e. study

design, epidemiologic context, health system integration) and then extracting from the relevant studies data for analysis (i.e. outcomes, cost and resource requirements for the intervention, comparator, targeted population and potential subgroups). Comparative analysis then evaluates potential interventions in terms of budget impact and how each meets the objectives of the HBP. Cost-effectiveness analysis (CEA) methods can inform the selection of interventions based on a stated objective, typically improving population health. This is followed by a deliberative phase (step 6) in which the results of the appraisals are considered by decision-makers and stakeholders. These discussions may also serve to redefine or clarify the social values underlying the HBP originally defined in step 1.

The deliberations will yield recommendations (step 7) that should then be communicated to policy makers at different levels of government and to the wider public – a key stage in ensuring that the HBP process is transparent and legitimate. Step 8 translates these recommendations into routine practice by allocating the real health resources to the services defined in the HBP over its life cycle. In step 9, the HBP is implemented, which requires management to ensure financial viability and institutional stability. This rollout should be monitored continuously to ensure that any issues are fed back to improve the HBP in the next planning cycle.

The policy cycle demonstrates how designing an HBP is both a technical and political undertaking [19]. Section 2 provides a brief overview of key principles relating to the politics and governance of HBPs. Section 3 provides a non-technical overview of the use of CEA in HBP design.

### 3. Governance and political considerations

#### 3.1 Governance

Good governance is important for successfully enacting the HBP policy cycle. Three key attributes have been identified in successful governance structures: transparency, consistent and stable processes, and participatory stakeholder involvement [20].

Transparency is an essential requirement if an HBP is to be accountable to the population it serves. This can be achieved through the provision of information on processes, responsibilities, analyses and results of the HBP to the general public and stakeholders. Ideally, this information should be relevant to these interested parties, readily available, shared in a standardised manner, up-to-date, and presented in an understandable way. In Colombia, for example, any changes made to the services included in the benefit package are transparently published in an online tool, enabling the public to hold the decision makers accountable when the HBP is updated [21].

The decision-making processes also need to be consistent, stable and coherent. Processes should not be arbitrarily changed, should not contradict each other, and should be logically ordered and intelligible. These attributes should help to ensure long-term commitment from all stakeholders, and allow for the fair and equitable treatment of all interest groups. Furthermore, stable processes can improve the accuracy of performance measurement and provide more amenable conditions for health sector investment. In Chile, for example, many aspects of the HBP are systematically reviewed each year, including the selection of benefits, costing exercises, the elicitation of social preferences and budget control [22]. By conducting this on a fixed-term basis, the Chilean Ministry of Health has created a stable and consistent process for managing the HBP.

Lastly, the HBP process should also include the systematic involvement of relevant stakeholders, including health professionals, insurers, health service providers, patients, civil society and the pharmaceutical industry. Different types of participation are possible including providing information, allowing consultation, active involvement and collaboration. In general, the degree of participation should reflect the role and interests of the particular stakeholder, with involvement limited to the relevant steps in the policy cycle. For example, consultation of medical technology and pharmaceutical companies may be unnecessary when defining social values and the objectives of the HBP, but could be useful at the evidence generation and appraisal stages.

#### 3.2 Political economy

Theories of political economy can help to analyse some of the political and social challenges associated with designing and implementing HBPs [20]. As the resources available for healthcare are inevitably limited, but demand is not, healthcare activities are always subject to rationing. These rationing decisions invariably involve negotiations between stakeholders, each of whom have incentives to direct the design and management of the HBP in line with their interests.

These issues can occur during each step of the policy cycle. Political economy theories highlight the following potential problems:

- **Veto points** describe the stages at which the progression of an HBP policy can be blocked by public institutions. Particular attention should be paid to how interest groups interact with these institutions, so called 'veto players', through processes such as hearings and consultations.
- **Historical institutionalism** helps to place the HBP process in the context of the pre-existing institutional structure of a society. The initial design of an HBP, as well as any subsequent

updates, should therefore be primed to negotiate resistance from those adversely affected from its implementation, for example, pharmaceutical companies or particular patient groups.

- **Bureaucratic actors** can also influence proceedings in ways not aligned with the broader public interest. An understanding of which actors are likely to be affected, as well as their personal incentives, can help to mitigate against this potential bias.
- **Political actors** may design policies aimed at ensuring electoral victories. This can skew the benefits of policies towards groups with higher voter turnout, often those of higher socioeconomic position, and impose more of the opportunity costs on less well represented groups.

The analysis of the political and economic context can help to ensure that HBP planners better understand the motivations behind influential stakeholders, and be equipped to mitigate the adverse effects that may arise from them. For example, in Costa Rica a pneumococcal vaccine (PCV) was included on the national vaccine list despite the national technical agency recommending against its inclusion. Investigations later showed that favourable studies were financed by the vaccine manufacturer and that the Minister of Health had received a donation to implement PCV campaigns [23].

## 4. Evaluating interventions for HBP

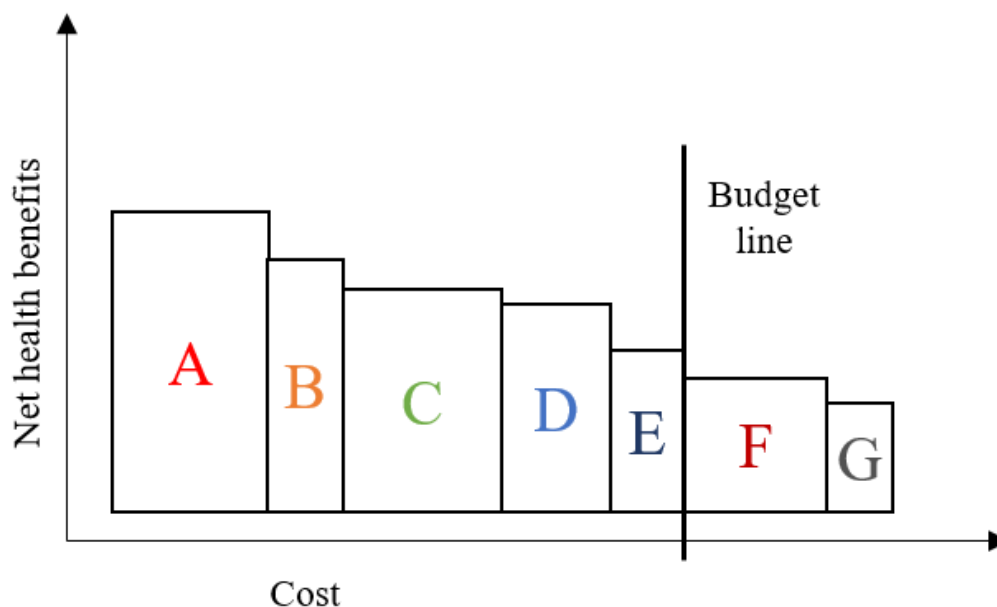
Determining which interventions should be provided in an HBP represents a major technical challenge. The objectives of the healthcare system can be diverse and differ from country to country. However, a central goal of nearly all health systems is to improve population health [24]. It is this central objective that has been a primary focus of methodological and applied research in health economics. The field of economic evaluation, and particularly the framework of CEA, provides a set of quantitative tools that estimate the effects of interventions on population health (see Appendix A for a primer in CEA). The evidence generated by such analyses can be useful for policymakers responsible for designing HBPs [25]. Health care systems may have additional objectives, such as improving access to care, increasing financial protection or reducing inequalities in health. Analytical methods for evaluating interventions in terms of these objectives have also been developed; for example, methods for incorporating inequality concerns into resource allocation decisions are discussed in a companion briefing paper [26].

The following sections describe some of the novel considerations that arise when moving from the commonly used ‘incremental’ application of CEA, in which a set of mutually exclusive interventions for a particular condition are evaluated and a decision made on which one to implement, to the context of an HBP, in which many interventions for different conditions are typically considered across the whole population simultaneously. We describe and discuss some of the issues regarding ‘decision rules’ for intervention selection and financial costing of packages. Familiarity with the basic concepts of CEA is presumed, which centre on net health benefit as a measure of value. Net health benefit represents the amount of health generated by an intervention less the health opportunity cost, i.e. the health which could be generated elsewhere using those same resources; for those unacquainted with CEA, an introductory overview is provided in Appendix A.

### 4.1 Cost-effectiveness analysis for HBP design

The most widely used application of CEA is to evaluate the adoption of an intervention as a ‘marginal’ decision. That is, on a case-by-case basis, to determine whether single interventions are added to the list of currently provided care [27]. For this approach to support decisions which are consistent with improvements in population health and financial sustainability, the additional health benefits of the appraised intervention for a particular patient group must be compared with an appropriate estimate of the opportunity cost that reflects how much health can be produced by using the same financial resource on other options for different patients.

An alternative method is the ‘bookshelf’ approach [28], which simultaneously identifies all interventions to be funded, by ordering the potential interventions from highest to lowest net health benefit. Starting with the intervention that provides the greatest net health benefit per person, interventions are selected until the budget is exhausted (demonstrated graphically in Figure 2). If the bookshelf approach is applied to all possible interventions and for all available healthcare resource, it determines how much health is produced with available resources. The informational requirements required to populate this bookshelf are vast, so it has not been widely employed in practice but is nevertheless a useful theoretical construct.



**Figure 2: Hypothetical health intervention 'bookshelf'. Interventions are funded in order of their net health benefit per person (bar height), until the available funds are exhausted (bar widths based on per person costs multiplied by the eligible patient population) in order to maximise the health generated from available resources. In this example, interventions A to E are included.**

As noted in section two, the amount of health sector resources that can be commanded by an HBP is determined by its shape (stage three). Specifying what to include in an HBP is likely to sit in between the 'marginal' approach and the fully exhaustive 'bookshelf' approach, appraising multiple interventions and populations in order to allocate a substantial (non-marginal) proportion of health sector resources. The consequence of this is that properties of both approaches may be utilised when applying CEA methods to HBP design. The set of interventions under consideration should be characterised in terms of their population health and cost impact and arranged on the 'bookshelf'. However, as the range of options may not be exhaustive of all health sector expenditure, the opportunity cost of including each intervention in the package should also be considered in terms of the value of potential other uses of health expenditure external to the HBP. These other uses can include investments in infrastructure that in themselves could enable different interventions to be delivered under the HBP [29].

The use of CEA methods in HBP design, therefore, presents some challenges not encountered in the methods as typically employed in, for instance, decisions on drug and intervention reimbursement made in high income countries. We group these into four categories: section 4.2 covers issues around the collection and use of relevant evidence; section 4.3 deals with decision rules; section 4.4 discusses recent research into modelling additional constraints more common in LMICs; and section 4.5 discusses the role of uncertainty.

## 4.2 Relevant evidence

Conducting CEAs and generating cost-effectiveness evidence is a resource-intensive process. Estimating the cost-effectiveness of all of the possible interventions that could be included in an HBP may itself not be feasible, or a cost-effective use of resources, for most LMICs. As a result, databases of cost-effectiveness evidence that can potentially be used to inform HBPs have been compiled. The three most prominent of these are the World Health Organization Cost-Effectiveness program (WHO-CHOICE) [30], the Global Health Cost-Effectiveness Analysis Registry by the Tufts Medical

Center [31], and the Disease Control Priorities (DCP) project [32]. Databases dedicated specifically to costing estimates, such as the Global Health Cost Consortium [33], can also be utilised.

The outcomes of interest from CEA studies are (i) incremental costs and (ii) incremental health effects compared to clear and relevant mutually exclusive alternatives. The cost impacts extend beyond treatment costs, and can include any related resource impacts. As these other costs can accrue many years after an intervention is delivered, incremental costs can differ markedly from the costs of funding an intervention in a given year (an issue discussed in more detail below). Health is measured using generic (rather than disease-specific) measures that account for changes to both health-related quality of life and survival – such as the quality-adjusted life year and the disability-adjusted life year. A more detailed overview of costs and health outcomes is provided in sections A3 and A4 of the appendix.

The use of these databases in the design of HBPs presents a number of issues [34]. Cost-effectiveness is often summarised in the form of the incremental cost-effectiveness ratio (ICER) and not in terms of the incremental health and cost that are used to derive it. The latter are crucial when used in the context of an HBP, as they can be combined with patient population figures to estimate the expected scale of health generated and costs from each intervention. Other relevant features of CEAs that are often not systematically reported in CEA databases include discount rates, time horizon and sensitivity analysis results.

Using these cost-effectiveness estimates in HBP design requires an assumption that they are generalisable between countries. However, each individual piece of evidence contributing to these estimates is specific to the context in which it was produced, and may not be generalizable to the health system of interest. This difference could be in the way in which the decision problem is characterised: the patient population may differ in disease severity or have a different age profile. Cost estimates will also differ between contexts, including when the availability of health services (i.e. to treat adverse events or complications) and the costs of different healthcare resources are different. These factors can have a considerable impact on the expected population health effect, and the use of non-generalisable (biased) results could result in incorrect decisions being made about which interventions to include in the HBP of any one jurisdiction. Caution should therefore be exercised when considering published cost-effectiveness results, and tools for assessing transferability should be used to generate locally relevant estimates, where possible [35], [36].

The scale of the population health impact of an intervention is partly determined by a comparison with what those patients would otherwise receive (the comparator(s)). As 'what patients would otherwise receive' differs from country to country, the choice of comparator intervention should match the situation in the health system of interest. This could depend upon whether the HBP specifies an entirely new list of interventions for delivery, or represents an incremental change to an existing package. With the former, the relevant comparator will be 'no intervention' (or 'do nothing'). With the latter, new interventions that would replace one or more that are already included in the package should be compared to those rather than 'no intervention'. In both cases, the new intervention should be the cost-effective option from a set of mutually exclusive alternatives (i.e. the one with the highest net health benefit). This can be derived by considering all the relevant options alongside one another in a fully incremental analysis (see Appendix A for a description of this procedure).

### **4.3 Decision rules for selecting interventions**

Assessment and collation of relevant evidence will yield a dataset containing information on the set of possible interventions to be included in the HBP. For the sole objective of maximising population health, three core pieces of information are required for each intervention: incremental benefit,

incremental cost, and patient population size. Incremental benefit and incremental cost should be in comparison to the relevant comparator (see above).

The first task is to calculate the cost-effectiveness of each intervention, expressed in terms of net health benefit. This measure explicitly incorporates the notion of health opportunity costs, the health that could otherwise have been gained by allocating resources elsewhere in the health system. An illustration of this process is provided in Table 1. This shows five hypothetical interventions, ordered in terms of their net health benefit per person. Health benefits are expressed in disability-adjusted life years (DALYs) averted and costs are converted into health opportunity costs at a rate of \$60 per DALY averted. This means that for every \$60 spent on the HBP, one DALY could be averted if it was spent on other health sector activities. We are able to eliminate intervention E entirely from consideration as it results in a reduction in population health at the given level of health opportunity cost (i.e. it generates less health than would be generated elsewhere with the same resources). Note that this can also be done by removing interventions with an ICER greater than \$60 per DALY averted, the health opportunity cost threshold ratio noted above.

**Table 1: Prioritisation of five hypothetical interventions**

Intervention	Comparator	Cost	Health benefit (DALY averted)	ICER	Net benefit
A	Do nothing	\$10	10	\$1	9.8
B	Do nothing	\$25	5	\$5	4.2
C	Do nothing	\$25	1	\$25	0.6
D	Do nothing	\$50	1	\$50	0.2
E	Do nothing	\$25	0.25	\$100	-0.2

**Note:** All values are expressed per patient; ICER = incremental cost-effectiveness ratio

The rate at which any costs associated with an intervention are converted into health opportunity costs depends on what type of services could have otherwise been funded with those same resources and their impact on health outcomes. This is an empirical problem that can be addressed by analyses of the overall marginal productivity of health systems [37]–[39]. These studies use advanced statistical methods that are beyond the scope of this review. However, they suggest that opportunity cost expressed as a ‘threshold’ cost-per-DALY averted is often much lower than levels previously recommended by the World Health Organization of 1-3 times GDP per capita. Sets of these empirically derived estimates are available for a range of LMICs in Woods et al. [40] and Ochalek et al. [38].

As well as deciding, which interventions do not appear to be a good use of limited resources, it is also necessary to clearly determine which interventions should be funded (based on the stated objective, in this case health maximisation). For this step, patient population numbers are used to scale up benefits and costs, the latter of which can be used to calculate how many interventions can be funded from within an overall budget envelope for the HBP.

This process is demonstrated in Table 2 for our previous sample of five (now four) interventions. Together, the interventions avert 1,155 DALYs at a cost \$20,125. We are now in a position to consider the budget constraint – the limit on health sector resources available to fund the HBP. If we suppose this budget constraint is \$5,000, then we can maximise population health by fully funding both A and B and partially fund C (up to 37%). This would result in a net population health gain of 1,048 DALYs averted. Intervention D, which has the lowest net health benefits of the four, is not allocated any funding. Since further net health benefits would be available by fully funding C & D, our analysis also suggests that additional funds should be transferred to the HBP and away from other activities in the health system, which have a higher cost-per-DALY averted.



**Table 2: Population-level impacts of five hypothetical interventions**

Intervention	Patient population	Cost (pp)	Net benefit (pp)	Cost (pop)	Cumulative cost	Net benefit (pop)
A	50	\$10	9.8	\$500	\$500	490
B	125	\$25	4.2	\$3,125	\$3,625	525
C	150	\$25	0.6	\$3,750	\$7,375	90
D	25	\$50	0.2	\$1,250	\$8,625	5

**Note:** pp = per patient; pop = population

In this simple optimisation we have assumed that the per patient cost of each intervention represents the annual costs that accrue to the health system, such that the total annual cost of the package aligns with its annual budget. However, the cost estimates from CEAs are reported for the time horizon of the analysis, which is often lifetime. As such, the intervention costs will be the net present (discounted) value of the cumulative costs over the life cycle of the treatment, and cost impacts from other health service use (i.e. cost savings from averted complications) can occur many years after initiating treatment.

Whilst these are the correct costs to use when generating the rank ordering of interventions, the allocation of the HBP budget to those interventions should instead be based on the actual financial cost to the health system over a given time period. This may necessitate a separate dedicated costing exercise, such as those described by Cashin and Özalın [41]. This can be a complicated task, as the delivery of an intervention in one year can result in additional costs (or cost savings) in subsequent years. Box 2 describes how these considerations, along with the many previous steps, were implemented in an analysis supporting the HBP that featured in the Health Sector Strategic Plan for Malawi for 2017-2022.

#### **Box 2: Use of cost-effectiveness methods to inform the Malawian Essential Health Package**

To help inform an update of Malawi's national health benefits package, the Essential Health Package (EHP), Ochalek and colleagues used cost-effectiveness methods to inform questions relating to intervention selection and health system investment [5]. These included the appropriate scale of the EHP, potential 'best buy' interventions, and the potential value of health system strengthening.

Information on health sector costs and health outcomes for 67 interventions were extracted from two cost-effectiveness databases (Tufts Cost-Effectiveness Analysis Registry and WHO-CHOICE). Each intervention was considered relative to what could have been achieved had the money been invested elsewhere in the health system. Using evidence-based estimates for Malawi [38], these health opportunities were generated at a rate of \$61 per DALY averted. The authors then costed a package including all interventions with positive net health benefits, using Malawi-specific drug and supply costs to reflect the financial costs to the health system. Expected levels of implementation were also calculated based on an analysis of bottlenecks in the Malawian healthcare system.

48 interventions were recommended for inclusion in the EHP, averting 49.5 million DALYs at a total cost of \$265 million. The total cost is reduced to \$67 million when the interventions are partially implemented to expected levels. Best buy interventions included HIV prevention strategies, maternal and child health interventions, and treatments for malaria and tuberculosis. The health gains associated with increasing implementation of the recommended interventions was estimated to be far greater than those that could be gained from expanding the package to include more interventions, suggesting that efforts to increase implementation levels should be explored.

The EHP that was ultimately implemented in Malawi was not determined solely on the basis of the CEA analysis, and at full implementation still exceeded the available Malawian health resources. However, value for money was increased: the package was costed at 69% of the previous EHP and was expected to deliver 92% of the health benefits.

Whilst our simple example can be conveniently calculated manually, mathematical programming approaches can automate the selection of interventions when there are a large number to choose from. This can be done through linear optimisation algorithms, more details of which can be found in Cleary et al [42], or other optimisation algorithms. The algorithms require the specification of an objective function and a set of constraints. In our example, the objective function is total population health benefit, with a constraint on the total cost. A variety of additional constraints and considerations can be incorporated into the mathematical programming approach, and are explored in the following section.

#### **4.4 Modelling additional constraints**

Certain features in many health systems may prevent the maximising of population health when selecting which health interventions to fund under an HBP. We explore two in this section: (i) ethical considerations; and (ii) human resource and health system constraints.

Incorporating equity concerns into CEA typically relates to issues such as health inequalities and financial protection, and have been described in a companion policy brief [26]. However, a range of additional equity considerations can also be directly incorporated into the optimisation framework described above in the form of constraints. For instance, the analysis in our stylised example (Table 2) recommended partially funding intervention C to maximise population net benefit. This systematic underfunding of a health intervention may be deemed unacceptable on equity grounds (e.g. horizontal equity by which all individuals with a condition should receive the same treatment may make the partial provision of it unacceptable). Adding an integer constraint such that an intervention must be provided at 100% or not at all would mean the algorithm would instead advocate intervention D. We may alternatively opt for a 'decent minimum' constraint, in which all patients receive treatment of some description, even if this means sacrificing the cost-effective option in order to fund less costly treatments with greater coverage [42].

Non-financial capacity constraints are also likely to be present within the health system, and will limit the extent to which interventions can be implemented. These can occur where access to services may be limited or there is a lack of critical assets such as human resources or facilities. The framework described in the previous section can be used to place a value on relieving these constraints, by using the patient population of the expected 'actual' implementation level rather than a hypothetical 'full' level [43]. The difference in net health benefit between the 'actual' levels and the full level can be used to help answer the question of whether health sector resources (including part of the HBP budget) could be better spent on relaxing these constraints and increasing implementation.

An example of this analysis is shown in Table 3, as applied to the hypothetical case from previous examples. The actual implementation levels are used to calculate the difference in DALYs averted between each intervention at actual and full levels of implementation. Across interventions, this equates to 1,475 DALYs averted. The economic value (at a rate of \$60 per DALY averted) of achieving full implementation across interventions is therefore \$88,500. This provides an estimate of the upper limit of spending on achieving full implementation that would be a cost-effective use of health sector resources.

**Table 3: Value to the health care system of scaling up interventions to full implementation**

<i>A</i>	<i>B</i>	<i>C</i>	<i>D</i>	<i>E</i>	<i>F</i>
Intervention	DALYs at actual imp.	Actual imp. level	DALYs at full imp. [ $B * 1/C$ ]	Full vs actual imp. [ $D - B$ ]	Value of actual to full imp. [ $E * \$60$ ]
<b>A</b>	490	50%	980	490	\$29,400
<b>B</b>	525	75%	700	175	\$10,500
<b>C</b>	90	10%	900	810	\$48,600
<b>D</b>	5	100%	5	0	\$0

**Note:** DALYs = disability-adjusted life years; imp = implementation

Analysing the cost-effectiveness of relaxing specific constraints within health systems is an area of active research. Theoretical approaches have been developed for a number of constraints, including human resources constraints and supply of labour [44], [45]; healthcare facilities [29]; and health system strengthening interventions that increase the effectiveness of multiple interventions at once (i.e. training programmes) [46]. However, few practical applications of these approaches have so far been published.

#### 4.5 Uncertainty

The inputs used to generate cost-effectiveness evidence are all inherently uncertain. Analyses supporting HBP design should reflect the potential impacts of this uncertainty. A simple approach to assessing the potential implications of uncertainty is to conduct deterministic sensitivity analysis, in which inputs or assumptions can be varied to examine the impacts on the cost-effectiveness results [47]. For example, varied inputs could include intervention cost, coverage rate, or target population size. These methods require a judgement on the likely range of uncertainty for each input, in order to produce an informative deterministic sensitivity analysis as the bounds are explicitly set by the analyst.

An alternative approach known as probabilistic sensitivity analysis varies all the inputs simultaneously. This involves assigning a probability distribution to each input; a set of values are drawn from these distributions and the analysis is rerun to estimate a new set of results. This process is then repeated many times. The results of each iteration are stored and can be used to quantify uncertainty in the results. In the context of an HBP, for instance, we would be able to estimate the probability that a particular intervention should be included in the benefits package [47]. This tests the overall robustness of the results and quantifies the degree to which results are reliable. The probabilistic analysis requires more data, such as information that can be used to define the probability distribution attached to each uncertain input.

The principal purpose of quantifying uncertainty is to help inform decision making. As well as yes/no decisions on interventions to include in an HBP, policy makers can also be required to assess uncertainty, and have the scope to recommend that available resources be used to fund research that reduces uncertainty and make better future decisions about which interventions to include in the package. Value of information (VOI) analysis is a quantitative approach that explores whether additional research is a worthwhile investment [42]. The core idea behind VOI is to explore the opportunity cost of research spending: whether the expected reduction in uncertainty from acquiring new evidence will justify its expenditure or would be better spent elsewhere. For an introductory overview to VOI, see Wilson [48].

## 5. Conclusion

This report summarises some of the key considerations and analytical approaches that can be utilised when designing and implementing an HBP. Good governance structures and an analysis of the political economy of the setting of the HBP can help health planners navigate the political and social barriers to implementation, whilst the tools of economic evaluation and cost-effectiveness analysis provide important evidence that aids the selection of the best possible set of interventions. These aspects fall under key stages in the HBP management cycle, a comprehensive set of processes that can help to ensure the efficiency, acceptability and sustainability of the HBP over time.

Although cost-effectiveness evidence is frequently claimed to have informed HBPs, rigorous and appropriate uses of these methods are still rare. This is in part due to CEA having been developed and applied to incremental (or marginal) decisions rather than to the more complex scenario of HBP design. This leaves scope for future research to improve the validity of cost-effectiveness evidence for HBP design, for instance through applied case studies investigating the effects of health system constraints or uncertainty.

It is also important to place cost-effectiveness evidence in its proper context within the HBP design process. The validity and reliability of the cost-effectiveness evidence is likely to be reduced in LMIC settings, where evidence generated from external health systems, with questionable transferability, is more likely to be used. The technical methods discussed in this brief should, therefore, be used to guide policy decision-making rather than automate it. This type of deliberative process forms a critical part of the HBP process and is a feature of many institutions that utilise cost-effectiveness evidence in some capacity. Decision-making committees can deliberate as to whether an intervention should be included in the package given the level of uncertainty in the technical analysis, the transferability of the evidence underpinning the technical analysis, as well as important ethical and political considerations.

HBPs are now seen as a methodical, transparent and explicit vehicle for improving the provision of healthcare to those with the highest need around the world. Utilising the insights of political and economic analysis that are highlighted in this brief can help to achieve this objective.

## 6. Further reading

### Cost-effectiveness analysis methods

- M. Drummond, M. J. Sculpher, K. Claxton, G. L. Stoddart, and G. W. Torrance, *Methods for the Economic Evaluation of Health Care Programmes*, 4th ed. Oxford: Oxford University Press, 2015.
- M. Sculpher, P. Revill, J. M. Ochalek, and K. Claxton, “How Much Health for the Money? Using Cost-Effectiveness Analysis to Support Benefits Plan Decisions,” in *What’s in, What’s out? Designing Benefits for Universal Health Coverage*, A. Glassman, U. Giedion, and P. Smith, Eds. Washington DC: Center for Global Development, 2017.

### Uncertainty in cost effectiveness

- H. Briggs, M. C. Weinstein, E. A. L. Fenwick, J. Karnon, M. J. Sculpher, and A. D. Paltiel, “Model Parameter Estimation and Uncertainty Analysis,” *Med. Decis. Mak.*, vol. 32, no. 5, pp. 722–732, Sep. 2012.

### Health system constraints

- P. van Baal, A. Morton, and J. L. Severens, “Health care input constraints and cost-effectiveness analysis decision rules,” *Soc. Sci. Med.*, vol. 200, no. August 2017, pp. 59–64, 2018.
- P. Revill, S. Walker, V. Cambiano, A. Phillips, and M. J. Sculpher, “Reflecting the real value of health care resources in modelling and cost-effectiveness studies — The example of viral load informed differentiated care,” *PLoS One*, pp. 1–13, 2018.
- K. Hauck *et al.*, “How can we evaluate the cost-effectiveness of health system strengthening? A typology and illustrations,” *Soc. Sci. Med.*, vol. 220, pp. 141–149, 2019.

### Health opportunity costs

- J. Ochalek, J. Lomas, and K. Claxton, “Estimating health opportunity costs in low- and middle-income countries: a novel approach and evidence from cross-country data,” *BMJ Glob. Heal.*, 2018.

### Health benefits package design

- Glassman, A., Giedion, U., & Smith, P. C. (Eds.). (2017). *What’s In, What’s Out? Designing Benefits for Universal Health Coverage*. Washington DC: Center for Global Development.

## 7. References

- [1] United Nations, Sustainable Development Goals, 2018. [Online]. Available: <http://www.un.org/sustainabledevelopment/sustainable-development-goals/>. [Accessed: 04-Apr-2018].
- [2] U. Giedion, R. Bitrán, and I. Tristao, *Health Benefit Plans in Latin America*, Inter-American Development Bank, 2014.
- [3] Y. Birtanov and V. S. Balakrishnan, Kazakhstan gears up to launch social health insurance, *Bull. World Health Organ.*, vol. 94, no. 11, pp. 792–793, Nov. 2016.
- [4] Government of the Republik of Malawi, Health Sector Strategic Plan II 2017-2022, Lilongwe, 2017.
- [5] J. Ochalek *et al.*, Supporting the development of a health benefits package in Malawi, *BMJ Glob. Heal.*, pp. 1–14, 2018.
- [6] National Hospital Insurance Fund, *Benefit Package - Explanation of the benefit package for the National Scheme*, NHIF, Nairobi, 2015.
- [7] M. Luwabelwa, P. Banda, M. Palale, and C.-C. C, A case study of the role of an Essential Health Benefit in the delivery of integrated health services in Zambia. Lusaka: Zambia Ministry of Health, EQUINET; 2017, Zambia Ministry of Health, EQUINET, Lusaka, *EQUINET Discussion Paper 111*, 2017.
- [8] R. Bitrán, Costeo de Planes de Beneficio En Salud, Inter-American Development Bank, Washington DC, 2012.
- [9] O. Cañón, M. Rathe, and Ú. Giedion, Estudio de caso del Plan de Servicios de Salud PDSS de la República Dominicana, Inter-American Development Bank, Washington, DC, 2014.
- [10] A. Glassman, U. Giedion, Y. Sakuma, and P. C. Smith, Defining a Health Benefits Package: What Are the Necessary Processes?, *Heal. Syst. Reform*, vol. 2, no. 1, pp. 39–50, 2016.
- [11] A. Phoya, T. Araru, R. Kachala, J. Chizonga, and C. Bowie, Setting Strategic Health Sector Priorities in Malawi, Department of Global Health, University of Washington, Seattle, Disease Control Priorities in Developing Countries, 3rd Edition Working Paper 9, 2014.
- [12] A. Brown, C. Zikusooka, and S. Bakeera, Development of the Minimum Service standards for Uganda's Health Sector: Final Report, Ministry of Health, Kampala, 2009.
- [13] I. Kadowa, Equity in Health in east A case study of the Uganda National Minimum Healthcare Package, Ministry of Health, EQUINET, Uganda, *EQUINET Discussion paper 110*, 2017.
- [14] Ministry of Health and Social Welfare, Health Sector Strategic Plan IV: July 2015 – June 2020, Dar es Salaam, 2015.
- [15] G. Todd, A. Nswilla, and O. Kisanga, Equity in Health in east A case study of the Essential Health Benefit in Tanzania Mainland, IHI, EQUINET, Tanzania, *EQUINET discussion paper 109*, 2017.

- [16] A. Glassman, U. Giedion, and P. C. Smith, The Health Benefits Package: Bringing Universal Health Coverage from Rhetoric to Reality, in *What's in, What's out? Designing Benefits for Universal Health Coverage*, A. Glassman, U. Giedion, and P. C. Smith, Eds. Washington DC: Center for Global Development, 2017.
- [17] G. Doran, There's a S.M.A.R.T. way to write management's goals and objectives, *Manage. Rev.*, vol. 70, no. 11, pp. 35–6, 1981.
- [18] Cochrane UK, What are systematic reviews?, 2019. [Online]. Available: <https://uk.cochrane.org/news/what-are-systematic-reviews>. [Accessed: 28-Mar-2019].
- [19] U. Giedion and J. Guzmán, Defining the Rules of the Game: Good Governance Principles for the Design and Revision of the Health Benefits Package, A. Glassman, U. Giedion, and P. C. Smith, Eds. Washington DC: Center for Global Development, 2017.
- [20] A. Glassman, Tough Choices: Considering Ethics, Rights, and Political Economy in Defining Benefits, in *What's in, What's out? Designing Benefits for Universal Health Coverage*, A. Glassman, U. Giedion, and P. Smith, Eds. Washington DC: Center for Global Development, 2017.
- [21] Todos Por Un Nuevo Pais and MinSalud, POS Pópuli, 2017. [Online]. Available: <https://pospopuli.minsalud.gov.co/PospopuliWeb/paginas/home.aspx>.
- [22] U. Giedion, Governance and Process: The Foundation of a Health Benefits Package Policy, in *What's in, What's out? Designing Benefits for Universal Health Coverage*, A. Glassman, U. Giedion, and P. Smith, Eds. Washington DC: Center for Global Development, 2017.
- [23] A. Glassman, O. Cañón, U. Giedion, and C. Vacca, ProVac Initiative Pan American Health Organization, Evaluation 2004–2013, Evaluation prepared for the Bill & Melinda Gates Foundation, 2014.
- [24] C. J. Murray and J. Frenk, A framework for assessing the performance of health systems., *Bull. World Health Organ.*, vol. 78, no. 6, pp. 717–31, 2000.
- [25] M. Sculpher, P. Revill, J. M. Ochalek, and K. Claxton, How Much Health for the Money? Using Cost-Effectiveness Analysis to Support Benefits Plan Decisions, in *What's in, What's out? Designing Benefits for Universal Health Coverage*, A. Glassman, U. Giedion, and P. Smith, Eds. Washington DC: Center for Global Development, 2017.
- [26] J. Love-Koh, S. Griffin, E. Kataika, P. Revill, S. Sibandze, and S. Walker, Incorporating Concerns for Equity into Health Resource Allocation: A Guide for Practitioners, Centre for Health Economics, York, CHE Research Paper 160, 2019.
- [27] M. Drummond, M. J. Sculpher, K. Claxton, G. L. Stoddart, and G. W. Torrance, *Methods for the Economic Evaluation of Health Care Programmes*, 4th ed. Oxford: Oxford University Press, 2015.
- [28] A. J. Culyer, Cost-effectiveness thresholds in health care: a bookshelf guide to their meaning and use, *Heal. Econ. Policy Law*, vol. 11, no. 04, pp. 415–432, 2016.

- [29] K. Hauck *et al.*, How can we evaluate the cost-effectiveness of health system strengthening? A typology and illustrations, *Soc. Sci. Med.*, vol. 220, pp. 141–149, 2019.
- [30] World Health Organization, WHO-CHOICE. [Online]. Available: <http://www.who.int/choice/cost-effectiveness/en/>. [Accessed: 03-Oct-2018].
- [31] The Center for the Evaluation of Value and Risk in Health and Tufts Medical Center, Cost-effectiveness analysis registry. [Online]. Available: <http://healthconomics.tuftsmedicalcenter.org/cear4/>. [Accessed: 02-Oct-2018].
- [32] DCP, Disease Control Priorities Project: Economic Evaluation for Health, 2013. [Online]. Available: <http://www.dcp-3.org/>. [Accessed: 19-Sep-2013].
- [33] The Global Health Cost Consortium. [Online]. Available: <https://ghcosting.org/>. [Accessed: 02-Oct-2018].
- [34] M. Arnold, S. Griffin, J. Ochalek, P. Revill, and S. Walker, A one stop shop for cost-effectiveness evidence? Recommendations for improving Disease Control Priorities, *Cost Eff. Resour. Alloc.*, vol. 17, no. 1, p. 7, 2019.
- [35] R. Welte, T. Feenstra, H. Jager, and R. Leidl, A Decision Chart for Assessing and Improving the Transferability of Economic Evaluation Results Between Countries, *Pharmacoeconomics*, vol. 22, no. 13, pp. 857–876, 2004.
- [36] M. Drummond *et al.*, Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report, *Value Heal.*, vol. 12, no. 4, pp. 409–418, 2009.
- [37] K. Claxton *et al.*, Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold, *Health Technol. Assess. (Rockv)*, vol. 19, no. 14, pp. 1–504, 2015.
- [38] J. Ochalek, J. Lomas, and K. Claxton, Estimating health opportunity costs in low- and middle-income countries: a novel approach and evidence from cross-country data, *BMJ Glob. Heal.*, 2018.
- [39] P. Thokala, J. Ochalek, A. A. Leech, and T. Tong, Cost-Effectiveness Thresholds: the Past, the Present and the Future, *Pharmacoeconomics*, vol. 36, no. 5, pp. 509–522, 2018.
- [40] B. Woods, P. Revill, M. Sculpher, and K. Claxton, Country-Level Cost-Effectiveness Thresholds: Initial Estimates and the Need for Further Research, *Value Heal.*, vol. 19, no. 8, pp. 929–935, 2016.
- [41] C. Cashin and A. Özaltın, At What Price? Costing the Health Benefits Package, in *What's In, What's Out? Designing Benefits for Universal Health Coverage*, A. Glassman, U. Giedion, and P. C. Smith, Eds. Washington DC: Center for Global Development, 2017.
- [42] S. Cleary, G. Mooney, and D. I. McIntyre, Equity and efficiency in HIV-treatment in South Africa: The contribution of mathematical programming to priority setting, *Health Econ.*, vol. 19, pp. 1166–1180, 2010.



- [43] R. Faria, S. Walker, S. Whyte, S. Dixon, S. Palmer, and M. Sculpher, How to Invest in Getting Cost-effective Technologies into Practice ? A Framework for Value of Implementation Analysis Applied to Novel Oral Anticoagulants, *Med. Decis. Mak.*, vol. 37, no. 2, pp. 148–161, 2017.
- [44] P. van Baal, A. Morton, and J. L. Severens, Health care input constraints and cost effectiveness analysis decision rules, *Soc. Sci. Med.*, vol. 200, no. August 2017, pp. 59–64, 2018.
- [45] P. Revill, S. Walker, V. Cambiano, A. Phillips, and M. J. Sculpher, Reflecting the real value of health care resources in modelling and cost-effectiveness studies — The example of viral load informed differentiated care, *PLoS One*, pp. 1–13, 2018.
- [46] A. Morton, R. Thomas, and P. C. Smith, Decision rules for allocation of finances to health systems strengthening, *J. Health Econ.*, vol. 49, pp. 97–108, 2016.
- [47] A. H. Briggs, M. C. Weinstein, E. A. L. Fenwick, J. Karnon, M. J. Sculpher, and A. D. Paltiel, Model Parameter Estimation and Uncertainty Analysis, *Med. Decis. Mak.*, vol. 32, no. 5, pp. 722–732, Sep. 2012.
- [48] E. C. F. Wilson, A Practical Guide to Value of Information Analysis, *Pharmacoeconomics*, vol. 33, no. 2, pp. 105–121, Feb. 2015.
- [49] E. J. Mishan and E. Quah, *Cost-Benefit Analysis*, 5th ed. Abingdon: Routledge, 2007.
- [50] K. Arrow, Uncertainty and the welfare economics of medical care, *Am. Econ. Rev.*, vol. 53, no. 5, pp. 141–149, 1963.
- [51] P. Dolan, C. Gudex, P. Kind, and A. Williams, A Social Tariff for EuroQol: Results from a UK General Population Survey, York, 138, 1995.
- [52] D. M. Epstein, Z. Chalabi, K. Claxton, and M. Sculpher, Efficiency, equity, and budgetary policies: informing decisions using mathematical programming., *Med. Decis. Mak.*, vol. 27, no. 2, pp. 128–37, 2007.
- [53] K. Claxton *et al.*, Probabilistic sensitivity analysis for NICE technology assessment: not an optional extra., *Health Econ.*, vol. 14, no. 4, pp. 339–47, Apr. 2005.

## Appendix – Primer on cost-effectiveness analysis

### A1. Introduction

Cost-effectiveness analysis is a form of economic evaluation that seeks to estimate the benefits and costs of different courses of action. In health care, it is used to estimate the health and resource impacts of health interventions. The objective is to provide evidence for decisions regarding the allocation of scarce health resources, and it has been a frequently used approach in health policy decision-making since the 1990s.

In fields outside of health, the most common form of economic evaluation is cost-benefit analysis. Under this approach, all outcomes of interest are converted into monetary units and compared with the costs [49]. However, the application of cost-benefit analysis to healthcare interventions is frequently cited as inappropriate, due to market failures in the demand and supply for health and healthcare, and the challenges of valuing health monetarily [50]. This has led to cost-effectiveness analysis, which typically evaluates interventions in terms of their health impacts, emerging as the predominant form of economic evaluation in the health sector.

This primer will cover four principal issues that present when planning a cost-effectiveness analysis: (i) the decision problem; (ii) outcomes; (iii) costs; and (iv) decision rules. For a more comprehensive overview of each topic and economic evaluation in health care more generally, see Drummond et al. [27].

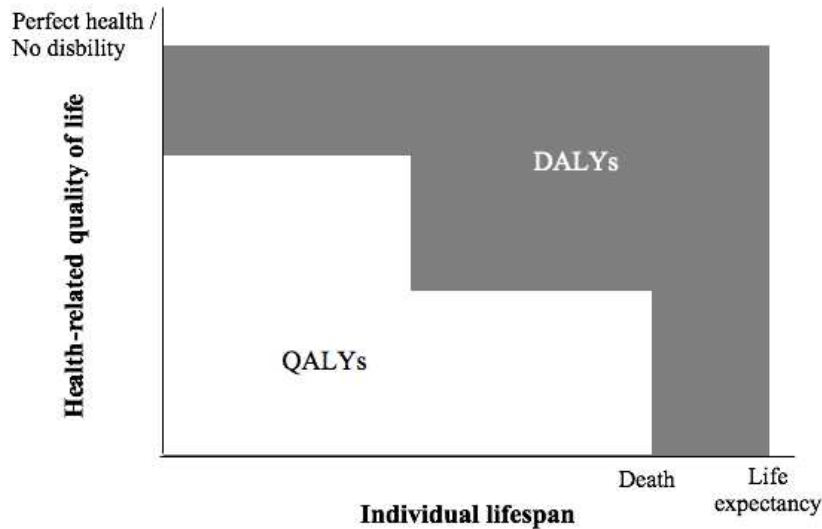
### A2. Decision problem

The decision problem is the specific research question that the analysis is seeking to address. For a given intervention, the two core components of the decision problem are the population and comparators. The population is typically the group of patients who will receive the intervention if it is introduced, which may be split into relevant subgroups (based on their disease severity, for instance).

The choice of comparator(s) to be included in an evaluation is not simply the best option currently available, but should include all the existing ways in which the population being considered may be treated – in other words, all ‘relevant’ comparators. A necessary requirement is that options being considered are mutually exclusive, in so far as providing one will preclude providing any of the others. Comparators can range from doing nothing to alternative interventions to a complex sequence of interventions. The costs and outcomes described in the following sections are estimated *incrementally* – how much more (or less) benefit and cost an intervention imposes, relative to what is currently done. This reflects the decision-making context faced in the high-income countries where health economic evaluation was initially developed.

### A3. Outcomes

Given the objective of health maximisation with the cost-effectiveness analysis framework, the outcome of interest is naturally a measure of health. Resulting from the need to be able to compare investments in interventions across different areas, a generic measure of health is needed, ideally one which incorporates information on two components: length of life and quality of life. This has led to the development of generic measures of health that quantify health-adjusted life years (HALYs), in which each year of life is adjusted downwards according to the level of morbidity experience during it. Two are commonly used in practice: the quality-adjusted life year and the disability-adjusted life year. These are illustrated graphically in Figure A1.



**Figure A1: The relationship between quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs). QALYs represent years of healthy life gained, whereas DALYs represent the gap between years lived in perfect health and years lived in less-than-perfect health**

Quality-adjusted life years (QALYs) are estimated using self-reported multi-attribute health questionnaires. Each specific combination of responses represents a health state, to which a pre-determined health related quality of life weight is assigned. These weights are derived from preference elicitation studies conducted in the population of interest, and are anchored at 1 for perfect health and 0 for dead. In England, the National Institute for Health and Care Excellence in England uses the EQ-5D questionnaire, which measures five dimensions of health: pain/discomfort, anxiety/depression, self-care, usual activities and mobility. A patient reporting moderate problems on all these dimensions for an entire year will be assigned 0.516 QALYs [51].

Disability-adjusted life years (DALYs) are calculated based on the presence of a disease or disease sequelae. DALYs have been more widely used in low- and middle-income countries (LMICs). As with QALYs, a set of estimated weights are attached to each disability state; however, contrary to QALYs, the weight represents the *loss* in health-related quality of life. An episode of severe diarrhoea, for example, has an associated weight of 0.247. This (and all other episodes of morbidity) will be subtracted from the individual's length of life to derive their disability-adjusted length of life. The difference between this and some maximum 'reference' life expectancy (i.e. the total health loss due to morbidity and premature mortality) are the individual's DALYs lost.

An intervention that improves health will, therefore, result in a gain in QALYs but will avert DALYs, as the latter is a measure of health loss. In subsequent examples we will not subscribe to either measure, and instead refer to generic health measures as health-adjusted life years.

#### **A4. Costs**

The relevant costs to consider within a cost-effectiveness analysis go beyond the financial costs required to directly fund the interventions under consideration. Introducing a new intervention may impose additional costs on the health sector (and other public sectors), and can have private cost implications for patients and their families or affect the economic productivity of patients.

From an economic perspective, costs are significant because they represent lost opportunities to invest the resources in other activities. In the economic evaluation of health interventions, these

opportunity costs can be quantified in terms of the health that could otherwise have been gained if the resources were used for other purposes. The rate at which costs are converted into health opportunity costs depends on productivity of the health system: more productive systems will have greater opportunity costs, as the alternative uses will generate more health. Research into health system marginal productivity has been an active area of research since 2015 [37]–[39].

Decisions about which costs to include are determined by the *perspective* of the analysis. The health sector perspective is commonly used and includes treatment costs and other health service use. The broadest perspective is the societal perspective, which includes all costs to society, including for example, private costs and productivity gains/losses. In order to maintain consistency between benefits and costs, any impacts estimated for the intervention should also be reflected on the opportunity cost side as well. For example, if an intervention generates productivity gains, then the productivity gains that could be otherwise generated by alternative interventions should also be accounted for.

Measuring the overall cost impact requires estimates of (i) the quantity of resources consumed and (ii) the monetary value of a unit of each resource (i.e. a bed day in hospital or GP visit). Quantities of resource use may be available from a variety of sources, for example, case records, administrative data or patient surveys. Monetary valuations can be obtained from market prices, although the market imperfections in healthcare mean that these should be treated cautiously. Reimbursement tariffs for hospitals can be used for pricing services where available. The cost of health sector workers should include overheads and training costs, in addition to salary costs.

## A5. Decision rules

The evidence on costs and outcomes is then combined to create measures of cost-effectiveness. A simple summary measure is the incremental cost-effectiveness ratio (ICER): the incremental costs of an intervention compared to a comparator, divided by the incremental benefits.

$$ICER = \frac{Cost_{Int} - Cost_{Comp}}{Health_{Int} - Health_{Comp}}$$

In a hypothetical situation in which the ICERs of all potential interventions were known, interventions would be funded in order from lowest (most favourable cost-effectiveness) to highest (least favourable cost-effectiveness) until healthcare resources were exhausted [52].

This type of approach is infeasible, from a practical perspective, in many of the high-income countries that have formally introduced cost-effectiveness analysis into healthcare decision-making. Instead, the approach has been to evaluate measures of cost-effectiveness with respect to a decision rule, from which it can be said that the intervention is likely to be cost-effective or not. This is broadly defined as the benefits outweighing the opportunity costs. When a health sector perspective is adopted, this means that the health benefits are greater than what would have otherwise have been funded.

A widely used method for determining the cost-effective intervention from a set of mutually exclusive options is to conduct a ‘fully incremental analysis’. This is a procedure that makes a series of pairwise comparisons between the options. First, any intervention ‘dominated’ by another – that it is more costly and less effective – is removed from the range of options. The remaining options are then organised from least to most costly, as demonstrated for four alternatives in Table A1 (interventions X, Y and Z and placebo).

**Table A1: Fully incremental analysis of three mutually exclusive options**

Comparator	Incremental cost	Incremental HALYs	ICER		
			vs Placebo	vs X	vs Y
Placebo	-	-	-	-	-
X	\$5,635	0.35	\$16,100	-	-
Y	\$6,954	0.375	\$18,544	\$52,760	-
Z	\$12,589	0.725	\$17,364	\$18,544	\$16,100

Note: Incremental costs and HALYs are calculated relative to placebo

An ICER is calculated for the least costly vs next least costly and compared to a threshold ratio representing the cost-per-HALY of what could otherwise have been funded (i.e the health opportunity cost). If the ICER is below the threshold ratio, more health is gained from the intervention than from other uses. If the ratio is above the threshold, the additional costs from the (more costly) intervention could have provided more health if spent on other activities.

The fully incremental analysis in Table A1, assuming a threshold ratio of \$20,000 per HALY, finds that Z is the cost-effective option. First, placebo is eliminated in a comparison with X with an ICER of \$16,100. Y is eliminated in a comparison with X as the ICER is well above \$20,000 (at \$52,760), and the comparison between X and Z yields an ICER of under \$20,000 (at \$18,544).

Cost-effectiveness can alternatively be expressed as net health benefit or net monetary benefit. These statistics use the same information as the ICER and directly incorporate the threshold ratio into the equation to account for health opportunity costs. For net health benefit (NHB), the incremental costs are converted into health opportunity costs by dividing through by the threshold ratio ( $\lambda$ ):

$$NHB = (Health_{Int} - Health_{Comp}) - \frac{(Cost_{Int} - Cost_{Comp})}{\lambda}$$

NHB therefore calculates the expected net improvement in HALYs from adopting the intervention. Net monetary benefit instead multiplies the health changes by the threshold ratio, calculating the net monetary value of the health benefits:

$$NMB = (Health_{Int} - Health_{Comp})\lambda - (Cost_{Int} - Cost_{Comp})$$

Both NHB and NMB are mathematically equivalent, with interventions being cost-effective if the net benefit is greater than zero. Table A2 recreates the cost-effectiveness summary of Table A1 using NHB instead of the ICER.

**Table A2: Fully incremental analysis of three mutually exclusive options using net health benefit**

Comparator	Incremental cost	Incremental HALYs	Net health benefit		
			vs Placebo	vs X	vs Y
Placebo	-	-	-	-	-
X	\$5,635	0.35	0.068	-	-
Y	\$6,954	0.375	0.027	-0.041	-
Z	\$12,589	0.725	0.096	0.027	0.068

## A6. Conclusion

This primer has described some of the central concepts and procedures of cost-effectiveness analysis. A considerable number of important features and discussion points relating to the approach were not covered. For example, the way in which uncertainty can be characterised and incorporated into the decision-making framework has been omitted. For a detailed discussion, see Claxton et al. [53]. Similarly, we have not discussed some of the fundamental assumptions underlying the fully incremental analysis procedure or the approaches for identifying and synthesizing relevant evidence (overviews of which can be found in Drummond et al. [27]). Readers with an interest in developing a deeper understanding of economic evaluation are encouraged to refer to these resources.