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Supporting the Development of an Essential Health Package: Principles and Initial Assessment for Malawi

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Abstract

Many health care systems in low income settings define essential health packages (EHP) to concentrate scarce resources on key health interventions to which their populations can have free access at the point of delivery. Malawi has used EHPs since 2004 but they have generally included unaffordable interventions that have not been fully delivered.

To guide decisions about the 2016 EHP in Malawi, an analytical framework is proposed that identifies interventions which, based on currently available evidence, offer the most gains in population health. The framework uses existing estimates of what the Malawian health care system is currently able to afford to generate gains in health – a measure of health opportunity costs. This facilitates an initial quantification of an appropriate budget for the EHP, and of the interventions that might be included which can then be prioritised on the basis of their expected impact on population health assuming 100% implementation.

In practice, lower levels of implementation will be achieved by interventions due to various constraints operating on the demand or supply side, and which apply to specific interventions or the system more generally. The framework provides an analytical basis to consider the implications for population health of these different types of constraints. It uses this as a basis of assessing how the underspend on the EHP due to the 'implementation gap' can be used. The framework estimates the potential impacts on health outcomes of intervention-specific implementation activities and system strengthening. These potential impacts are compared with the health outcomes offered by extending the package to include additional interventions.

The analytical framework can also assess the implications for population health of the types of constraints that donors may impose on their funding schemes in health care. These constraints can include requiring that particular interventions are included in the EHP when the funding could have a bigger impact on health if spent elsewhere; offers to expand the package but restricted to particular interventions and forgoing greater health outcomes elsewhere; and offers to provide additional funding as long as these are matched by government. In negotiating with donors and communicating with relevant stakeholders, policy makers will benefit from understanding the implications for population health of such constraints.

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1. Policy context and purpose

Malawi has had an Essential Health Package (EHP) since 2004. The criteria employed to determine which interventions within programmes to include have resulted in an unaffordable package that is only available and free at the point of care on paper. In reality there are significant gaps in the coverage of essential interventions, with parts of the country, particularly rural areas, able to offer only very limited and uncertain access for those in most need. This also places those seeking essential care, which in reality may be unavailable within the public system, at significant financial risk.

The 2011-16 package used a prioritisation strategy based on disease burden and cost-effectiveness, but without proper consideration of what the Malawian health system was able to achieve with existing levels of available expenditure (health opportunity costs). The resulting recommended package – if fully implemented – would have required substantially more public resources than were, or could have been, made available to Malawi's Ministry of Health. In addition, the mix of selected interventions and programmes did not properly prioritise within the package or reflect on likely levels of implementation due to supply and demand constraints. It also included some interventions where the resources required (even if they had been available) could have had a greater impact on health if they had been devoted to interventions and programmes that were excluded or not fully implemented.

To support decisions regarding the 2016-21 package requires an analytical framework that can support a decision making process focused on improving health outcomes overall. This requires available evidence on the costs and health effects of candidate interventions to be identified, together with empirical evidence on health opportunity costs that reflects what Malawi is currently able to afford to pay to improve health (cost per DALY). Together, this evidence can be used to rank candidate interventions within programmes for the EHP in terms of their overall likely impact on population health.

Inevitably, there are constraints on the levels of implementation that are feasible for EHP programmes. Some of these constraints operate at the level of the specific intervention or programme: constraints on the supply side (e.g. limited skilled staff) and demand side (e.g. travel distance for patients and/or adherence to treatments). Other constraints relate to the health system, again on the supply side (e.g. unreliable availability of power and water) and demand side (the ability to raise public finance to support spending Ministries including Heath). Comparing the impact of programmes on population health with and without these constraints provides an indication of the maximum gains of efforts to relax constraints and strengthen the health care system. This can inform decisions about using some of the resources available for the EHP (or making more resource available from outside the EHP) for system strengthening, such as investment in infrastructure and assuring effective supply of products and training of skilled labour.

Analysis is needed which also helps decision-makers understand and communicate the implications of donor-imposed constraints and guide their policy responses. This framework provides an estimate of the gains in population health that would be possible if the Ministry of Health had an unconstrained choice of which interventions it includes in the EHP. It provides a baseline against which to compare the effects of donor-imposed conditions on population health, rather than allowing the additional donor funds to be used for whatever intervention or implementation activity the available evidence suggests will generate the greatest impact on health outcomes.

Decision-makers may also wish to consider a range of objectives in addition to gains in population health, e.g. interventions which promote financial protection more than others or to reduce health inequalities. If evidence is available, the analytical framework could be extended to include these other considerations. A primary focus on health can, however, inform decisions about the inevitable trade-offs with other objectives, and more political considerations, based on changes in population health.

2. Informing health care decisions: the importance of health opportunity costs

To decide whether an intervention will improve health outcomes overall and should be regarded as cost-effective, a comparison is required with an assessment of the likely health opportunity costs. This is commonly described as a comparison with a 'cost-effectiveness threshold'. Much of the published literature of such thresholds, and the values recommended, reflect a lack of conceptual clarity. None represents what is required: an evidence based assessment of the likely health opportunity costs.

Recent research has demonstrated that an empirical assessment of health opportunity costs is possible based on estimates of the health effects of changes in health care expenditure. Empirical work has been extended to low- and middle-income countries (LMICs) reflecting factors such as their demography, epidemiology, health care expenditure and income.

Such cost-effectiveness 'thresholds' are not decision 'rules' but provide a benchmark to search for and identify other under exploited investments that could offer greater value, and existing commitments that could be disinvested to accommodate more valuable ones. Such estimates ensure that decisions based on cost-effectiveness analysis improve rather than reduce health outcomes overall.

An assessment of the likely health opportunity costs makes it clear that health care costs matter because they represent the opportunity to improve the health of others who could benefit from health care. An empirical assessment of health opportunity costs makes the strong ethical foundation of cost-effectiveness analysis less abstract and more easily communicated to the range of stakeholders. This can help make the politically difficult decisions of what programmes and interventions can be included in the EHP (and which cannot) a more accountable, evidence based and, therefore, sustainable prospect.

Existing evidence of the effect of changes in health expenditure on health outcomes has been marshalled in recent studies to inform an assessment of health opportunity costs in LMICs. This research suggests that the cost per DALY is typically lower (health opportunity costs are typically higher) in lower income settings. The GDP per capita-based thresholds that have become widely used to judge cost effectiveness in LMICs are likely to be significantly higher than an assessment of health opportunity costs.

Estimates of health opportunity costs are presented that indicate what the current evidence suggests Malawi is currently paying to avert a DALY. Once the health that is likely to be delivered by greater health care expenditure is set out, it then becomes possible to have a more meaningful deliberation about how Malawi's public finance resources might be allocated between competing claims and how increases in public finance might be achieved.

3. Supporting the development of an EHP in Malawi

An analytical framework is developed and illustrated, and its implications for the Malawian EHP considered. In developing this framework, the best data currently available has been brought

together, but this can be improved upon and extended over time. The main purpose is to show the principles of the analytical framework, how it can guide a range of important policy questions and its implications for the EHP based on currently available evidence. A series of analytical steps is taken:

The appropriate scale of the EHP. This is initially based on the empirical estimates of health opportunity costs in Malawi (cost per DALY). This provides a means of identifying candidate programmes for the EHP that are expected to generate health at a cost that is consistent with what Malawi can currently afford. The cost of these candidate programmes provides information on the size of the budget that might reasonably be devoted to the EHP. On the basis of an estimated health opportunity cost of $61 per DALY averted, 48 of the candidate programmes can be afforded. Together, and assuming full implementation, these would cost $264.5 million per annum that can be considered an appropriate budget for the EHP. The framework allows the total costs and health effects, if Malawi could afford to pay more (or less) to improve health (a higher or lower cost per DALY), to be considered.

Maximising gains in population health from the available budget. Ranking of interventions is not possible based on their cost per DALY estimates. Rather it needs to consider the health gains for the population that can benefit from an intervention net of the health opportunity costs of the total resources required to deliver it (net DALYs averted).

Informing decisions regarding implementation and system strengthening. The impact on population health of the programme-specific and system-level constraints that result in an 'implementation gap' is reported. The magnitude of the budget underspend associated with less than full implementation is also presented.

Prioritising programme-specific implementation activities. A range of policy options exist to address the constraints facing specific programmes that result in less than full implementation, and can relate to the demand side or supply side. Prioritisation of such activities by programme is informed by the magnitude of loss in population health net of health opportunity cost (net DALYs averted).

Informing policy on system-level constraints and system strengthening. The framework provides an indication of the maximum potential value of system strengthening and can support decisions regarding whether such policies should be prioritised over programme-specific activities. This can be considered alongside the underspend on the budget due to partial implementation but reflecting the fact that, although longer-term health benefits may be realised from a stronger health system, there would be no *immediate* health gain if all the EHP underspend was devoted to system strengthening.

Accepting current levels of implementation and funding additional programmes. Rather than using the underspend on the EHP budget due to partial implementation on implementation activities and system strengthening, it could, instead, be devoted to extending the package by including additional programmes that were initially excluded. The framework presents the additional programmes that could be included at realistic implementation levels, and the impact on population health, i.e., simply accepting existing constraints and system weaknesses.

Assessing the implications of donor-imposed constraints. The framework also considers the implications for population health of another type of constraint – those imposed by donors. Four types of donor constraint and their potential health opportunity costs are considered: a requirement that a particular programme is included in the EHP (when a bigger impact on health outcomes is possible if the resources where spent elsewhere); an offer to expand the package but restricted to a particular programme (when greater health outcomes could be generated by spending elsewhere); an offer to provide additional funding as long as this is matched by the

Malawian Ministry of Health and conditional on the funding going on a particular programme; and an offer to provide additional funding as long as this is matched with additional health care expenditure, but without a condition that the funding goes on a particular programme.

4. Establishing and implementing an Essential Health Package

Given that a number of the key considerations in developing the EHP are subject to rapid change over time, there is a strong case for the Malawian Ministry of Health to provide more frequent assessment of the scale of the package, the interventions to be included and the funding of intervention-specific implementation activities and system strengthening.

The framework uses currently available evidence on the health opportunity cost and the costs and effects of the range of candidate interventions for the EHP. International work on health opportunity costs relevant to individual jurisdictions is central to evidence-based resource allocation decisions, and providing a more precise estimate for Malawi is likely to be a priority research area. The evidence on the costs and effects of potential EHP interventions used in the framework to date needs further development.

It is important to emphasise that the analytical framework and the results it has generated so far **is not** to specify a list of interventions that ought to be included in the EHP. Rather, this analysis is intended to support the decision making process of the Ministry of Health. It can be used to engage with a range of relevant stakeholders and more effectively communicate the difficult choices, inevitable trade-offs and considerations to wider communities.

1. Policy context and purpose

1.1 Essential Health Packages in Malawi

Malawi has had an Essential Health Package (EHP) since 2004 (Appendix 1 provides a brief summary of the plans and how they were developed). The initial version (2004-9) focussed on reducing infant and under-five mortality, improving maternal mortality rates, preventing HIV and reducing population growth. The revised package, developed in 2011, sought to use disease burden and 'cost-effectiveness' as a basis of expanding the EHP interventions for non-communicable diseases and some surgical procedures. The criteria employed for this expansion, however, resulted in an unaffordable package as it was estimated to cost 83-132% of total health expenditure across the five years of the package (Appendix 1). This has resulted in a package that is only theoretically available and publicly funded for those who need it. In reality local availability has been limited, as stocks of relevant products have been exhausted as financial resources run out.

The challenge of achieving an affordable and sustainable EHP in the 2011-16 period requires a careful consideration of the lessons to learn from the criteria that were employed in defining that package. A prioritisation strategy was developed that, firstly, identified potential interventions relating to diseases with high burden; a second strand to the strategy considered what was termed 'cost-effectiveness'. Neither element of this strategy, however, directly considered the overall impact of interventions on overall population health factoring in the health outcomes the Malawian health system was already able to achieve from its expenditure (health opportunity costs).

Initial prioritisation using disease burden identified disease areas affecting large populations, interventions for which had potentially high budget impacts but would not necessarily impact significantly on burden. The cost-effectiveness aspect of prioritisation failed to consider the rate at which the Malawian health sector was already generating gains in population health. This resulted in a recommended package that – if fully implemented – would have absorbed too great a proportion of Malawi's overall health care resources and diverted too much funding away from interventions that could generate greater health outcomes than those recommended (i.e. the health opportunity costs would have been considerable).

1.2 Prioritising the 2016 Essential Health Package: development of a framework

It is important to learn from the limitations of the 2011 methods and to develop an appropriate framework for guiding decisions about the EHP in 2016. This framework would put the objective of increasing overall population health at the centre of defining an EHP. This requires the use of best evidence on the costs and health effects of interventions. It also needs to use available empirical evidence on health opportunity costs that reflects the rate at which the Malawian health system is currently able to generate health improvement from its expenditure. This evidence-based assessment will mean that estimates of cost-effectiveness can better inform prioritisation decisions, and that these decisions improve - rather than reduce - health outcomes overall (Drummond et al., 2015).

1.2.1 Determining what interventions enter the EHP

An appropriate analytical framework to guide decisions needs to establish a set of candidate interventions. This should be informed by the available empirical evidence on what Malawi is currently able to afford to improve health. That is, the rate at which Malawi is currently able to translate its public expenditure on health care into heath improvements for its population. To consider including interventions in the EHP that require more expenditure to improve health than the overall system currently needs would not make sense: it would make less effective use of resources and reduce population health. Similarly, to limit the EHP only to interventions that require

lower expenditure to generate health outcomes than the overall system would be inappropriate because Malawi could afford to allocate more funding to the EHP and improve overall population health.

The framework would then be able to prioritise these candidate interventions for the package. This is achieved by establishing a ranking, based on available evidence, in terms of impact on population health. This needs an assessment of the magnitude of health gain for the average patient over and above how much health improvement could have been generated with the same level of public expenditure elsewhere in the system (i.e. the average patient's health outcomes net of health opportunity cost). This *net health effect* per patient is then scaled by the size of the recipient population; the larger the overall number of patients who stand to benefit from an intervention, the greater the overall impact on population health.

The framework would make clear the implications for population health of devoting more or less overall funding to the EHP. There is inevitable uncertainty associated with empirical estimates of what Malawi can currently afford to pay for health care. However, by running different scenarios regarding this estimate, it is possible to show the implications for the interventions that could be included in the package, the implied EHP budget, and the gains in population health associated with expected levels of implementation of those interventions.

1.2.2 Implementation levels and enhancement

Ideally a given intervention would reach the entire patient population that stands to benefit from it. In reality, however, there are constraints on the levels of implementation that are feasible for EHP interventions (Mills (1994) and Hanson et al. (2003)). Some of these constraints operate at the level of the specific intervention. On the 'supply side', the health system may, for example, have a limited number of specific skilled staff or a shortage of appropriate equipment. On the 'demand side', patients may fail to initiate or to continue a treatment from which they are expected to benefit, perhaps due to an associated social stigma. Other constraints relate to the health system more generally and impact on the implementation of all interventions. Such 'system weaknesses' might include, on the supply side, unreliable availability of power and water, inefficiencies or bottlenecks in the procurement of products, and a lack of hospital beds or clinic space. On the demand side, system-level constraints might relate to the travel distance patients have to make to access care.

An analytical framework seeking to support decisions about an EHP needs to incorporate realistic rates of implementation for each candidate intervention. This provides an estimate of health outcomes that are feasible based on expected levels of implementation. This estimate can be compared with the health outcome that is expected to be achieved in the absence of supply or demand side constraints – that is, the health gains from removing the 'implementation gap' and all patients ultimately receiving the interventions for which they are eligible (Fenwick, Claxton and Sculpher, 2008). This comparison is important to guide decisions because it provides an indication of the maximum gains in population health that would be achieved if policies were available to remove all supply and demand side constraints to take implementation to 100%. This shows to decision makers the maximum potential value of investing resources system strengthening policies - such as investment in infrastructure, assuring effective supply of products, and training of skilled labour – that can increase implementation across interventions in the EHP.

Furthermore, the maximum potential gains in population health from policies to remove gaps in implementation will vary across interventions. The magnitude of these gains will depend on the per-patient net health effects (allowing for health opportunity costs) and the absolute number of patients who are not receiving the intervention that is appropriate for them. These estimated maximum potential gains for individual interventions inform decisions regarding whether to invest in intervention-specific initiatives to increase implementation and how to prioritise across

interventions. On the demand side these implementation activities may include conditional cash transfers to patients to incentivise update and adherence. On the supply side possible policies may involve staff training or the purchase of equipment. If less than full implementation of one or more interventions is related to a failure by districts or providers to organise services appropriately, consideration could be given to how to incentivise those organisations to deliver EHP interventions.

These examples indicate that many of the policies to address supply and demand side constraints – at a system or intervention level – involve investments that draw on financial resources from the EHP budget. This may not be the case for all implementation-enhancing activities – for example, donors or central government might be willing to fund system strengthening from outside the package. The implementation gap not only results in lower levels of population health than could be achieved with 100% implementation of interventions, it also means the EHP budget is underspent. Some proportion of this underspend can be allocated to increase implementation. Making clear the maximum potential gain in population health associated with removing the implementation gap (at intervention and system level) provides an initial indication of the scale of benefit from implementation-enhancing activities and system strengthening. Ultimately, however, best available evidence on the costs and effectiveness of specific activities will need to be assessed to determine whether any such investment is funded and, if so, which particular types of implementation initiative or health system strengthening receives this funding.

Such assessments might conclude that implementation and system strengthening activities are not feasible or that their costs cannot be justified on their expected impact on population health. It may then be appropriate to retain existing interventions at less than 100% implementation and to use the budget underspend in adding interventions to the EHP. Expected gains in population health by extending the package in this way can be contrasted with what would be possible if full implementation of a more restricted package had been feasible.

1.2.3 Examining donor-imposed constraints

An analytical framework to guide EHP decisions should also provide a basis to understand the implication of donor-imposed constraints and to guide policy responses. Following the principles outlined above, this can be achieved by using best evidence to estimate the gains in population health associated with the Malawian Ministry of Health having an unconstrained choice of which interventions it includes in the EHP. This provides a 'baseline' against which to compare the effects of donor-imposed conditions on population health. For example, a donor may be willing to provide additional funding for the EHP but only on a specific intervention which, available evidence suggests, is not sufficiently effective given its additional cost to be included in the EHP with the existing budget or an increased one through the donor contribution. The framework can then quantify the cost to population health of the donor imposing a particular intervention on the EHP rather than allowing the health system to use additional donor funds to invest in whatever activity or intervention the available evidence suggests will generate the greatest impact on overall health.

Such an analysis comparing the health benefits of the donor's proposal with the health opportunity cost can inform a discussion with donors about the need to impose constraints on their funding, and to engage stakeholders in understanding the implications of particular policy options regarding donor offers. Such options would include accepting the donor proposal but being clear about the health opportunity costs of doing so; rejecting donor funding with constraints thus avoiding the damage of the imposed intervention but losing the benefit that could be achieved with donor funding; and accepting the proposal but using policies to mitigate the worse effects of the donor-imposed constraints (e.g. use of user fees to deter uptake of the imposed intervention).

1.2.4 Arrangements between the national EHP and districts

The analytical framework can be conceptualised to guide national decisions about which interventions to include in the EHP and the commensurate level of budget, and to guide decisions about implementation activities, system strengthening, and donor proposals. The framework can also provide a guide to the choice of policies regarding the role of districts in delivering the EHP. Districts will vary according to the needs of their populations for interventions within the EHP, and the framework provides a means of quantifying the financial resources that will need to flow from the centre to each district to fund EHP interventions given levels of need.

The constraints discussed above that prevent full implementation of the interventions are also likely to vary between districts. Furthermore, the balance between intervention-specific factors and system weaknesses that explain the implementation gap are unlikely to be the same for each locality. The analytical framework can guide Ministry of Health policies regarding implementation at the district level. In particular, there will be a balance to strike between the objectives of the funding that flows from the centre to the districts. That funding should reflect district-specific levels of need, but may also take as given the local system's expected levels of implementation that may be markedly less than 100%, reflecting intervention-specific and system-level constraints.

As at the national level discussed above, there is also scope to use the underspend from less than 100% intervention implementation at local level to address intervention-level constraints or to invest in system strengthening. Such investments may seek to incentivise more extensive implementation of the EHP; for example, by making funding for system strengthening conditional on evidence of improved implementation of EHP interventions. By making the net impact on population health explicit, the analytical framework can help to shape an evolving resource allocation mechanism between the Ministry of Health and districts.

1.2.5 Considerations other than health

Inevitably, the Ministry of Health and stakeholders may want to consider a range of objectives in addition to gains in population health when making decisions about what interventions to include in the EHP. These might include, for example, using interventions to promote financial protection or to reduce health inequalities, and recognising the impact of interventions on wider social objectives such as productivity. In principle, it is possible to extend the measure of benefit and opportunity cost to include these other considerations (Asaria, Griffin and Cookson (2015) and Verguet, Laxminarayan and Jamison (2015)). In practice, this may be challenging based on available evidence, in which case it is possible to inform decisions about relevant trade-offs based on changes in population health (Drummond et al., 2015).

As discussed, a framework based on the objective of changes in population health will consider the health benefits of a specific intervention and the health opportunity costs associated with its cost at realistic levels of implementation. If a decision maker is considering the inclusion of an intervention in the EHP that cannot be justified in terms of gains in population health (e.g. due to anticipated gains in wider social benefits), the implications of such a decision for net health outcomes should be clear. In other words, the decision making associated with the selection of interventions for the EHP will inevitably need to consider a range of factors; the analytical framework can provide a clear quantification of the health opportunity costs associated with such a decision. The transparency associated with this trade-off should support the accountability of funding decisions.

1.3 Guide to this report

The next section of this report develops the keys concepts around health opportunity costs, describes the emerging empirical evidence relating to these metrics and shows how important they are in guiding resource allocation decisions.

Section 3 describes the analytical framework that has been developed to inform decisions about the selection of interventions for the EHP in Malawi. It uses available data to draw out insights into which interventions are consistent with increasing population health. Finally, Section 4 offers some conclusions and comments on how the framework can contribute to decision making in Malawi.

2. Informing health care decisions: the importance of health opportunity costs

2.1 Introduction

Decision makers in all countries (whether low, medium or high income), face difficult decisions about how to use the resources available for health care to achieve the greatest improvement in agreed social objectives. They also need to decide how much of the available resources should be devoted to health care.

An important objective of health care expenditure is to improve health itself, which includes improvements in survival and reductions in morbidity. This requires an assessment of whether the improvement in health outcomes offered by investing additional resources in an intervention (which may be a technology, a service or a whole pathway of care) exceeds the improvement in health that would have been possible if the resources required had, instead, been made available for other health care activities. Therefore, some assessment of these health opportunity costs is required if the best use is to be made of available resources.

Methods of analysis to estimate the expected costs and health effects of the range of alternative interventions available to improve the health of a specific population with a particular indication are well developed (Drummond et al., 2015). The results are commonly summarised as incremental cost-effectiveness ratios (ICERs), which provide a useful summary of how much additional resource is required to achieve a measured improvement in health (e.g. the additional cost per Disability Adjusted Life Year (DALY) averted), or how much health is delivered for an amount of resource (e.g. the DALYs averted per $1,000).

However, to decide whether the intervention will improve health outcomes overall (and should be regarded as cost-effective) a comparison is required with an assessment of the likely health opportunity costs. This is commonly described as a comparison with a cost-effectiveness threshold (Drummond et al., 2015). To date much effort has been devoted to assessing the incremental costs and effects of interventions but there remains much confusion about what a cost-effectiveness threshold ought to represent and what type of evidence might inform its assessment. As a consequence much of the published literature and the values recommend or cited by decision making and advisory bodies (both national and supra national) reflects a lack of conceptual clarity (see Section 2.4). None represent what is required; an evidence based assessment of the likely health opportunity costs (Revill et al. (2014) and Culyer (2015)).

Recent research has demonstrated that an empirical assessment of health opportunity costs is possible based on estimates of the health effects of changes in health care expenditure (Claxton et al., 2015a). This has been extended to estimating health opportunity costs for LMICs (Woods et al., 2015), reflecting their demography, epidemiology, health care expenditure, income and other characteristics (Ochalek, Lomas and Claxton (2015)). It is now possible to make real what was previously an abstract concept (see Section 2.3). An assessment of health opportunity costs in Malawi can support decisions about which programmes and interventions might be included in an EHP, what the scale of the EHP might be and how efforts to implement interventions might be prioritised. It also allows the health opportunity costs of the other constraints that decision makers face (including restrictions placed on assistance by donors) to be identified. These assessments can be used to prioritise aspects of health care system strengthening and negotiate more effectively with donors on how their assistance can best meet Malawi's health care needs.

2.2 The role of health opportunity costs

An explicit and evidence based assessment of health opportunity costs means that estimates of cost-effectiveness can better inform prioritisation decisions. Most importantly it ensures that decisions based on cost-effectiveness analysis improve rather than reduce health outcomes overall. It also makes it possible to directly compare the health benefits and health opportunity costs of an intervention. The expected net health benefits (net DALYs averted) represent the potential net health impact of ensuring an intervention is fully implemented. The value of the intervention can also be expressed in monetary terms as the amount of additional health care resources that would be equivalent to the net health benefits it offers (the $ value to the health care system).

2.2.1 The importance of health opportunity costs

The importance of an assessment of health opportunity costs is illustrated in Figure 1, based on a stylised example of a new intervention (T1) compared to existing provision (T0 = no active treatment) for a specific population[1]. The new intervention offers additional health benefits of 200,000 DALYs averted, if fully implemented, at an additional cost of C1=$20mn. Therefore, the intervention offers one DALY averted for every additional $100 spent. Although this is a useful summary of the cost-effectiveness of T1 compared to T0, the key question is whether or not the additional 200,000 DALYs averted justify the additional $20mn required. An estimate of health opportunity costs of $200 per DALY is represented by the rising diagonal in Figure 1. Since every $200 of health care resources could be used to avert one DALY, the addition costs of $20mn could, instead, have been used to avert 100,000 DALYs elsewhere in the health care system.

The health benefits of 200,000 DALYs averted can be directly compared to the health opportunity costs of 100,000 DALYs. The intervention offers positive net health benefits of 100,000 DALYs averted and should be regarded as cost effective because it will improve health outcomes overall. Equivalently, the value of the intervention can be expressed as the amount of health care resources that would be required to generate the same health benefits elsewhere, e.g. $40mn would be required to avert 200,000 DALYs. The $ value of the intervention to the health care system ($20mn) is the difference between the monetary valuation of the additional health benefits ($40mn) and the additional costs ($20mn). Reporting cost-effectiveness in these ways is entirely equivalent to asking whether the ICER for alternative T1 is less than a threshold that represents health opportunity costs. However, an assessment of health opportunity costs allows the results of cost effectiveness analysis to be expressed in ways that can more directly inform prioritisation and development decisions (see Section 2.2.2).

An assessment of health opportunity cost is required whether or not additional costs must be found from existing resources or from increases in health expenditure that could have been used in other ways. Therefore, an assessment of health opportunity cost that represents what a health care system could have delivered with more or less resources (i.e. a supply side estimate of the marginal productivity of the health care system, see Section 2.3) is required, whether or not there are explicit administrative health care budgets and whether or not there are restrictions on the growth in health expenditure.

This is also a key question when considering whether more resources should be devoted to health care. For example, it is not possible to sensibly consider how much should be spent on an activity without some assessment of what is likely to be gained from that expenditure. In the context of health care that requires an assessment of the likely productivity of the health care system, i.e. an

[1] Commonly there will be a number of alternative mutually exclusives available including the option of offering no care for a specific indication and target population. The principles illustrated in Figure 1 and Table 1 generalise to a full incremental analysis of multiple alternatives, which should not be restricted to existing provision (Drummond et al., 2015), see Appendix 2.

assessment of what a health care system currently delivers with more or less resources (see Section 2.3).

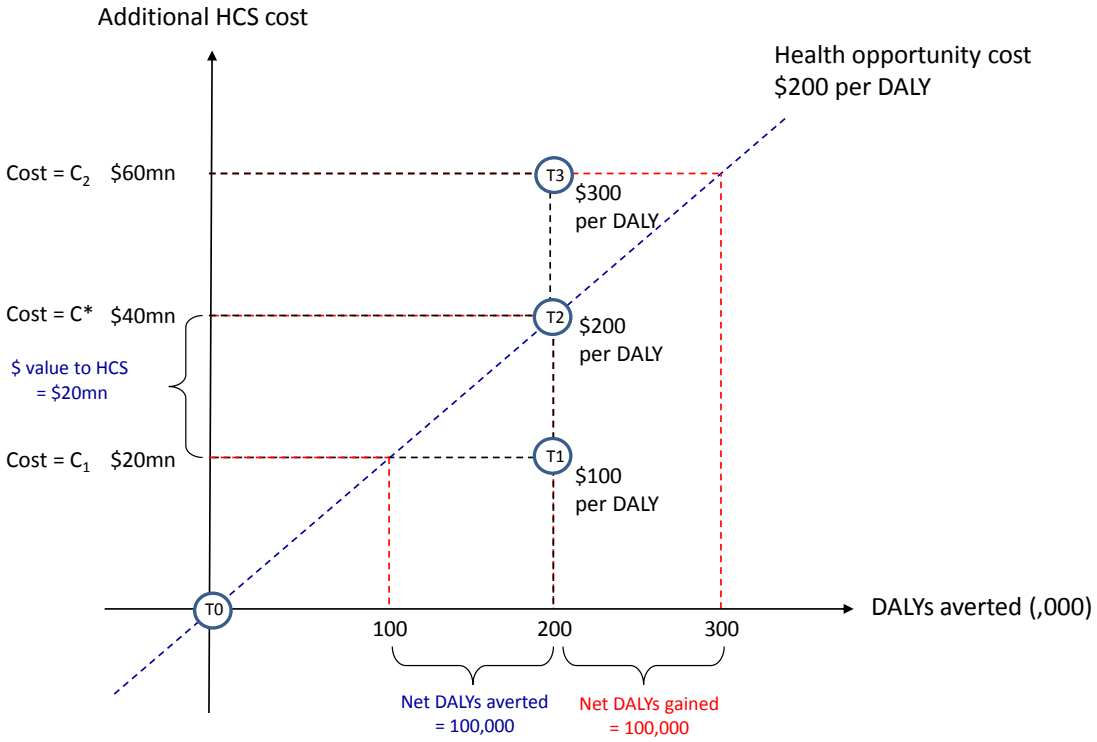


Figure 1 Cost-effectiveness and health opportunity costs

Consequences of adopting a 'threshold' that is too high

The consequences of using a 'threshold' that is too high to judge cost-effectiveness can be illustrated in Figure 1. If the costs of the intervention were higher (C2=$60mn), the new technology (T2) would offer one DALY averted for every additional $300 spent. This would be regarded as cost-effective at higher thresholds (e.g. at a threshold of $500 per DALY, which might represent GDP per capita). However, the health opportunity cost of these additional costs (300,000 DALYs) exceeds the health benefits. Concluding that the intervention is cost-effective, including it in the EHP and/or prioritising its implementation, will reduce rather than improve health outcomes overall (a net loss of 100,000 DALYs). This illustrates the dangers of adopting 'thresholds' that represent a particular view of what value ought to be placed on health (see Section 2.5) rather than an assessment of what the health opportunity cost are likely to be given the resources currently available (see Section 2.3).

Adopting 'thresholds' which are higher than the likely health opportunity cost also underestimates the health that could be gained by increasing health care expenditure. An explicit and evidence based assessment of health opportunity costs exposes the implications of the resources currently available and the real value of increasing them. It contributes to greater accountability in low and middle, as well as in high-income countries, for the health care and other expenditure decisions made at a local, national and supra national levels.

Informing purchasing and pricing decisions

An assessment of health opportunity costs demonstrates that the price paid for a technology is just as important as how effective it might be. In Figure 1, an additional cost of C*=$40mn represents the maximum the health care system can afford to pay for the benefit the technology offers (at C* the net DALY averted and the $ value to the health care system are zero). This can inform pricing and purchasing decisions by identifying the maximum price that a health care system (HCS) can afford to pay for a technology that is protected by patent, e.g. a branded pharmaceutical. Different health care systems are likely to face different health opportunity costs so the maximum, or value based, price of a branded pharmaceutical will differ (e.g. it is likely to be much lower in Malawi than in South Africa or even in other LICs, such as Mozambique). This assessment can be used to inform evidence based tiered pricing mechanisms, which respect patent protection, and inform value based purchasing negotiations. It also identifies the value of more effective purchasing of other health care inputs and the most that might be offered as incentives to encourage implementation, e.g. through 'payment by results' mechanisms (see Section 2.2.2).

Supporting decision making

Estimates of the health effects of changes in health care expenditure indicates health effects of other care that is likely to be offered if the required increase in expenditure was, instead, made available for other uses, or the health likely to be forgone if the additional resources required must be found from existing commitments. It is a measure of the amount of health that a health care system currently delivers with more or less resources, i.e. a supply side measure of the marginal productivity of health care expenditure (see Section 2.3).

These types of estimates can support decision making by providing a useful benchmark against which the likely overall health impact of the range of potential investment and/or disinvestment decisions can be judged. It indicates the health effects of the other investments or disinvestments that are likely to be made elsewhere (rather than could be made) when more or fewer resources are available. Such cost-effectiveness 'thresholds' are not decision 'rules' but provide a benchmark to search for and explicitly identify other under exploited investments which could offer greater value, and existing commitments that could be disinvested to accommodate more valuable ones (the resources released could be used to avert more DALYs). As well as informing the content and scale of an EHP, an assessment of health opportunity costs based on estimates of the health effects of changes in expenditure can also inform the incremental reallocation of resources which can strengthen a health care system and improve health overall.

There are also other constraints, (e.g. skilled labour, budgetary silos, political considerations etc.) which may mean that a cost-effective and valuable intervention cannot be fully implemented. The net DALYs averted and the $ value to the HCS indicates the opportunity cost of existing constraints, the value of addressing them and how strengthening these aspects of the health care system might be prioritised (see Section 2.2.2). Health and how it is measured (DALYs) is unlikely to be the only social objective of health care expenditure (e.g. others might include improving equity etc.). An assessment of health opportunity costs allows the sometimes necessary trade-offs to be identified and explicitly considered (e.g. when considering whether to include an intervention in a benefits package that might not be judged cost-effective but would offer significant benefits to disadvantaged groups).

A cost-effectiveness threshold based on an assessment of the likely health opportunity costs makes it clear that health care costs matter because they represent the opportunity to improve the health of others who could benefit from health care. Although the direct beneficiaries of an intervention might be more readily identifiable compared to those who will ultimately bear the health opportunity costs, there appears to be no reason to treat those who are more easily identifiable differently from those who are not. An empirical assessment of health opportunity costs makes the

strong ethical foundation of cost-effectiveness analysis less abstract and more easily communicated to the range of stakeholders. This can help make the politically difficult decisions of what programmes and interventions can be include in the EHP (and which cannot) a more accountable, evidence based and, therefore, sustainable prospect.

2.2.2 Prioritising implementation

An assessment of health opportunity costs makes it possible to express cost-effectiveness as the expected additional net health or net monetary benefit offered. This provides much more useful information than a categorical assessment of whether or not an intervention is cost-effective (see Appendix 2)[2]. It indicates the scale of the potential overall impact of ensuring an intervention is fully implemented and identifies the amount of resource that might be devoted to these efforts.

For example, in Figure 1 and in Table 1 an intervention T1 with costs of C1=$20mn would be regarded as cost-effective. Its full implementation would offer substantial net health benefits of 100,000 DALYs averted so it might be prioritised for additional implementation efforts. The $ value to the HCS of $20mn indicates an upper bound on the resources that might be devoted to this; for example, by addressing constraints which might not be fully reflected in the costs (e.g. labour constraints) or aspects of health system strengthening that might be required. An intervention T2 offering the same health benefits but with additional costs of C*=$40mn might also be judged to be cost-effective (the cost per DALY of $200 is equal to the 'threshold'). However, the health opportunity costs of 200,000 DALYs are equal to the additional health benefits it offers. Its full implementation will neither improve nor reduce health outcomes overall (net DALYs averted are zero) so it should not be prioritised because any additional resources required would reduce health outcomes overall.

Table 1 Prioritising implementation efforts

Technology	ICER ($/DALY)	DALYs averted (,000 DALYs)	HCS Costs	Net DALYS averted (,000 DALYs)	$ Value to HCS
T3	$300	200	$60m	-100	-$20m
T2	$200	200	$40m	0	0
T1	$100	200	$20m	100	$20m
T4	-$100	200	-$20m	300	$60m

Interventions which save health care costs can be judged and prioritised in the same way, rather than simply categorising them as cost-effective. For example, an intervention (T4 in Table 1) that offered the same health benefits but also saved $20mn of health care costs would have greater value because the saved resources would be available for other health care activities. These would be expected to avert 100,000 DALYs elsewhere (i.e. there are health opportunity 'gains' rather than costs). The net DALYs averted would be greater (300,000 DALYs averted) because they include the additional benefit of the technology (200,000 DALYs averted) plus the health opportunity 'gains' (100,000 DALYs averted)[3]. Similarly the $ value to the HCS is greater ($60mn) because it includes the amount of health care resources that would be required to generate the same health benefits elsewhere ($40mn), plus the saving of $20mn.

An assessment of net DALYs averted and the $ value to HCS enables prioritisation of implementation efforts among those interventions which are cost saving. It also ensures that all interventions,

[2] Cost per DALY measures cannot be used to rank interventions by the value they offer or indicate the scale of value (in DALYs or $). Therefore, cost per DALY cannot be used to prioritise implementation efforts. The examples of technologies T1 –T4 in Table 1 are a simple special case where the scales of population health benefits are the same. See Appendix 2 for examples where cost-per DALY is especially misleading because the population that can benefit from each technology differs.

[3] This can also be represented graphically in the south west quadrant of Figure 1.

whether cost saving or not, are prioritised in the same way based on the scale of the impact on overall health outcomes. This is especially important because the value (in DALYs averted or $) of interventions which require additional health care resources can be greater than those that save costs. Similarly, an intervention with an ICER that is higher than others may offer greater net DALYs averted or $ value to HCS so might be a higher priority for implementation efforts. An assessment of health opportunity costs makes it possible to estimate the scale of the potential impacts on overall health outcomes of implementation efforts in a way that reporting ICERs and categorical judgments about cost-effectiveness do not (see Appendix 2)[4].

2.3 Estimating health opportunity costs

The problem of estimating a cost-effectiveness threshold that represents expected health opportunity costs is the same as estimating the relationship between changes in health care expenditure and health outcome. This is the approach that was taken in research conducted in the UK.

2.3.1 Recent estimates for the United Kingdom

This research used national data on expenditure and outcomes in different areas of disease (programme budget categories) reported at a local level in the UK NHS (Claxton et al., 2015a) (Martin, Rice and Smith, 2008). By exploiting the variation in expenditure and mortality outcomes, the relationship between changes in spending and mortality was estimated while accounting for endogeneity[5]. With additional information about age and gender of the patient population, the estimated mortality effects were expressed as survival effects (£25,241 per life year) which were adjusted for health related quality of life. By using the effect of expenditure on the mortality and life-year burden of disease as a surrogate for the effects on a more complete measure of burden (one that also includes the quality of life burden of disease), a cost per QALY threshold that reflects the likely impact of expenditure on both mortality and morbidity was estimated (£12,936 per QALY).

This cost per QALY threshold is founded on estimating the health effects of changes in expenditure in 23 different disease areas (groups of ICD codes). Therefore, as well as identifying the scale of health opportunity costs, it also indicates how they are likely to be made up including the type of health effects (e.g. mortality, survival and morbidity), and where these are likely to occur (e.g. which disease areas and by age and gender). As a consequence, it is also possible to estimate the severity of disease associated with the health opportunity costs, how they are likely to be distributed, and the impact of changes in expenditure on health inequality (Claxton et al., 2015b) (Love-Koh et al., 2016).

Other work by the UK Department of Health estimated the net production effects for the wider economy of changes in length and quality of life by age, gender, and type of disease. This enabled the net production impact of changes in health expenditure (including marketed and non-marketed activities) to be estimated (Claxton et al., 2015b). More recent work has explored the impact of the scale of changes in expenditure on health outcomes, i.e. how the scale of budget impact and questions of affordability effect health opportunity costs. The UK Department of Health is supporting the ongoing re-estimation of cost per QALY thresholds for subsequent waves of data, which will provide a time series of estimates.

[4] When there is more than one active intervention available within a programme (a specific indication for a specific population) the use of cost per DALY is even more problematic. An assessment of health opportunity costs which enables measures of the net DALYs averted and $ value to HCS overcomes these difficulties (see Appendix 2).

[5] Health outcomes in a particular disease area are influenced by expenditure (increases in expenditure improves outcomes), but outcomes also influence expenditure (poor outcomes prompt greater efforts and increased expenditure).

2.3.2 Possible implications for other countries

The research conducted in the UK represents the first estimate of what a health care system currently delivers with more or fewer resources given the scale of total health care expenditure, i.e. a supply side estimate of its marginal productivity. It reveals how much the UK health care system can afford to pay to improve health given how much of available national income has been devoted to health care e.g. £12,936 per QALY in 2008/09 represented 48% of UK GDP pc.

Woods et al. (2015) explores the possible implications that this might have for other countries with different incomes. Published research has explored how the value placed on improvements in health vary with income, based on how much consumption individuals are willing to give up to reduce mortality risk from cross sectional and longitudinal studies. A smaller literature has examined how these estimates of income elasticity of demand might be applied across countries. Insofar as what heath care systems can deliver (the supply side) is consistently related to measures of the consumption value of health (an indication of the demand for health), estimates of income elasticity can be used to extrapolate the estimates reported in Claxton et al. (2015b) to other countries.

In general, the range of estimates of income elasticity suggests that a greater proportion of income is likely to be devoted to health care as income rises. This suggests that cost-effectiveness thresholds for countries with substantially less income than the UK are unlikely to be greater than 48% of GDP pc. For example, the range of estimates for Ethiopia, a country with a GDP pc of $505, is $10-$255 per QALY, or 2%-50% of GDP pc; and for Indonesia, with a GDP pc of $3,457, it is $472-$1,786 per QALY, or 14%-51% GDP pc (all in 2013 US$).

These ranges do not reflect all sources of uncertainty. For example, there is uncertainty associated with the UK estimate of £12,936 per QALY, and the alternative estimates of income elasticity are based on the value of reducing mortality risk rather than improvements in survival and reductions in morbidity[6]. Importantly, however, it must also be assumed that any proportionate 'underfunding' of health care from collectively pooled resources, compared to individual preferences about health and consumption, is similar across countries, i.e. the supply side of health care systems are related to measures of the demand for health in a similar and consistent way. The difficulties faced in financing health care systems in low income countries are well documented and suggests that 'under funding' is likely to be proportionately greater, so cost-effectiveness thresholds are likely to be lower in these settings. However, where donor funding represents a significant component of health expenditure, and any substitution effects are partial, then the proportional 'underfunding' maybe be offset by this assistance and the cost-effectiveness threshold may be higher.

Although the estimates reported in Woods et al. (2015) are based on limited data and uncertain assumptions, it is not clear a priori whether these are likely to lead to over- or under-estimates of thresholds that represent the likely health opportunity costs in LMICs. They do, however, provide indicative estimates which attempt to draw out the possible implications of the limited evidence that is available.

2.3.3 Estimates of the effect of expenditure on mortality outcomes

The effect of different levels of health care expenditure on mortality outcomes has been investigated in a number of published studies using aggregate country level data (Nakamura et al., 2016). The challenge is to control for all other reasons why mortality might differ between countries

[6] The morbidity adjusted survival effects of changes in mortality risk are likely to vary across countries with different GDP pc. Where the morbidity adjusted survival effects of changes in mortality are believed to be lower, the cost per QALY threshold will be higher. Although life expectancies tend to be lower in lower income settings, mortality tends to occur at younger ages so the net effect on cost per QALY thresholds is unclear.

to isolate the causal effect of differences in health expenditure. This is a particular challenge even if available measures are complete, accurate and unbiased because health expenditure and other key variables (e.g. GDP pc) are likely to be endogenous[7]. A number of published studies have used instrumental variables to overcome this problem and identify the mortality effect of different levels of health expenditure.

For example, Bokhari, Gai and Gottret (2007) apply this approach to a cross-section of 127 countries to estimate the proportionate effect (on maternal and under 5 mortality) of proportionate changes in health expenditure (they estimate elasticities). They account for the endogeneity of public health expenditure and GDP per capita, and also allow changes in donor funding and measures of infrastructure to influence the mortality effects of expenditure. In their re-evaluation of this analysis, Nakamura et al. (2016) find that while the estimates are somewhat sensitive in magnitude, qualitatively the model estimates are robust.

Ochalek et al. (2015) demonstrate how these types of estimates can be extended to include the likely impact on length and quality of life (measured by DALYs), reflecting a country's demography, epidemiology, level of health care expenditure, income and other characteristics. For example, Bokhari et al. (2007) can be extended to estimate the effect of expenditure on adult male and female mortality. The estimated elasticities can be expressed as a cost per life year gained using country specific estimates of mortality rates, conditional life expectancies and population (all by age and gender), as well as the level of total health expenditure. These country specific estimates of cost per life year can be expressed as a cost per DALY averted based on estimates of morbidity (years of life with disability) and assuming that the mortality effects of expenditure is a reasonable surrogate for the likely morbidity effects. These 'indirect' estimates of the cost per DALY use other data and explicit assumptions to link directly estimated mortality effects to survival and morbidity (in a similar way to the analysis in Claxton et al. (2015a)). Ochalek et al. (2015) are also able to directly estimate survival effects, disability effects and DALY effects of changes in expenditure by re-estimating the statistical model using data on years of life lost (YLL), years of life with disability (YLD) and DALYs for each country.

Ochalek et al. (2015) provide a number of cost per DALY estimates for each country, which enables a comparison of indirectly estimated effects on survival and disability (e.g. when only mortality data is available) to directly estimated effects on DALYs. In general, estimating DALY effects indirectly from changes in mortality does not necessarily lead to over or underestimation of cost per DALY averted. This suggests the framework of analysis set out in Ochalek et al. (2015) can be applied to the results of any econometric study thought to identify plausible effects on mortality of changes or differences in health expenditure. The difficultly is identifying effects of health expenditure on mortality using aggregate country level data given the challenges of endogeneity, limited and sometimes weak instruments, missing data and measurement error (Nakamura et al., 2016).

2.3.4 Summary of evidence for cost per DALY thresholds

The estimates reported in Woods et al. (2015) and Ochalek et al. (2015) show how existing evidence of the effect of changes in health expenditure on health outcomes can be marshalled to inform an assessment of health opportunity costs in LMICs. The range of estimates of a cost per DALY for each LMIC[8] based on Woods et al. (2015) and Ochalek et al. (2015) are reported in Figure 2 by GDP pc. The ranges from these two different sources are, in broad terms, reasonably consistent. They suggest that the cost per DALY is typically lower in lower income settings (health opportunity costs are typically higher) and are very likely to be lower than one GDP pc.

[7] See Footnote 5.

[8] Countries that were classified as a LMIC in 2000.

The range of estimates of cost per DALY thresholds for each country is reported in Figure 3 by under 5 mortality rates. As expected the cost per DALY is likely to be lower for countries with higher under 5 mortality, so increases in expenditure in these contexts are likely have greater health effects. This relationship does not simply reflect any negative correlation between under 5 mortality and GDP pc[9], but reflects different absolute effects of changes in expenditure in countries with different baseline mortality rates, demographics and total health care expenditure, as well as different relative effects in countries with different levels of infrastructure and donor funding.

Although the estimates from Woods et al. (2015) and Ochalek et al. (2015) rest on a number of assumptions and judgements, including the robustness of different underpinning research (e.g. Claxton et al. (2015a) and Bokhari et al. (2007) respectively), they both indicate broadly similar implications of the balance of existing evidence. In particular, they suggest that the type of GDP pc based thresholds that have become widely used to judge cost-effectiveness in LMICs (see Section 3.2) are likely to be significantly higher than an assessment of health opportunity costs, e.g. the cost per DALY may be less than half GDP pc for most health care systems. However, the results from Ochalek et al. (2015) also suggests that expressing cost per DALY in terms of GDP pc might not be the best way to summarise how health opportunity costs are likely to differ between countries. GDP pc is clearly important but mortality rates, demographics, total health care expenditure, as well as donor funding and infrastructure, are also important. Rather than adopting a simple summary, based only on GPD pc, Ochalek et al. (2015) show that country specific estimates, which reflect the interaction of all these factors, are possible.

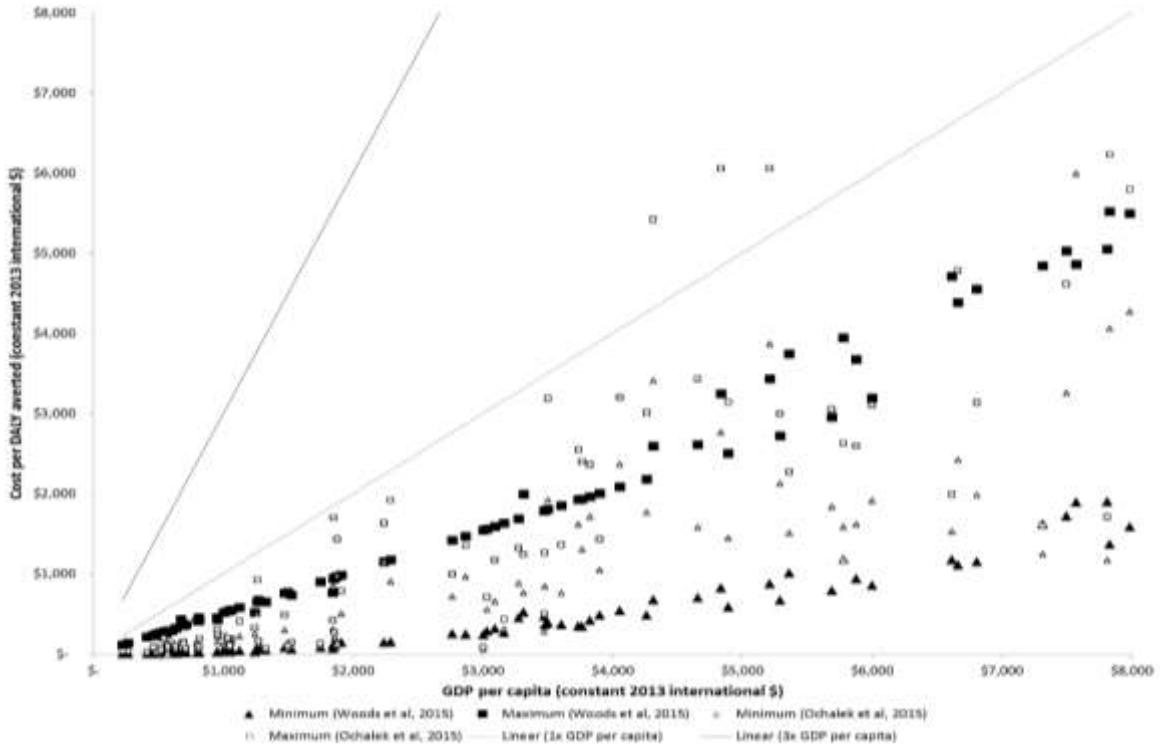


Figure 2 Cost per DALY ranges for Woods et al. (2015) and Ochalek et al. (2015) by GDP pc

[9] The estimates from Woods, B., et al. (2015) would simply reflect any negative correlation of under 5 mortality and GDP pc, so have been excluded from this figure.

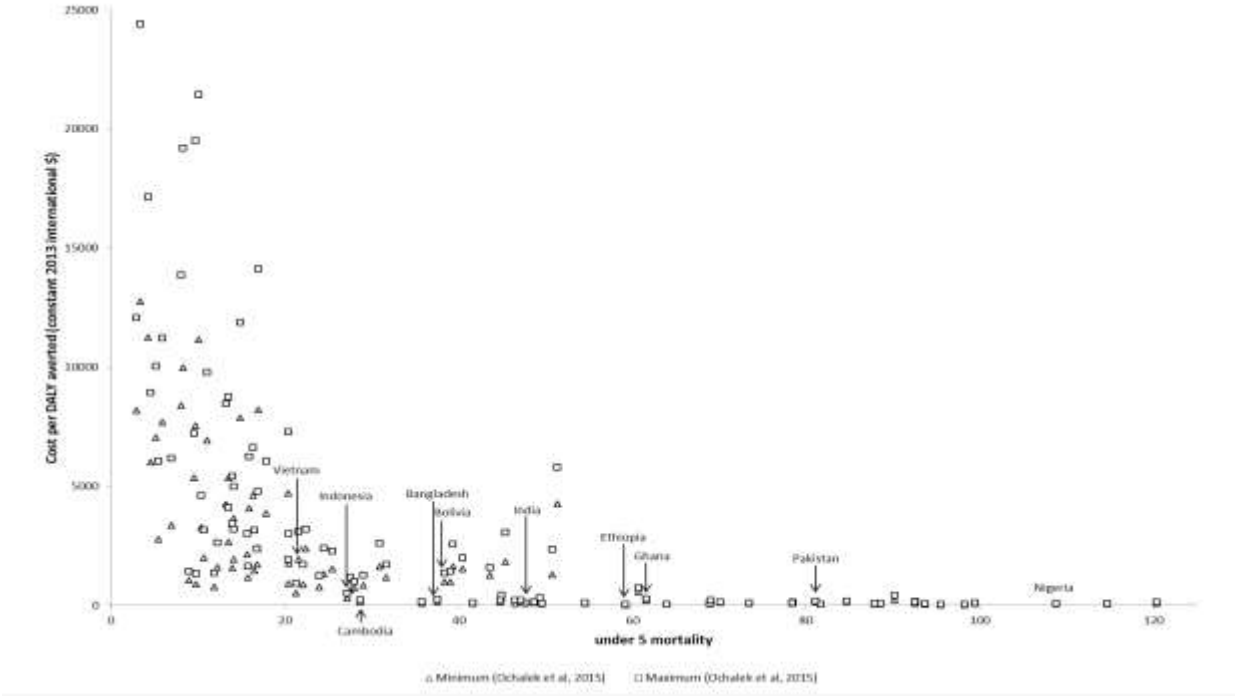


Figure 3 Cost per DALY ranges from Ochalek et al. (2015) by under 5 mortality

Any empirical approach to estimating the effect of health expenditure on health outcomes is especially challenging when using aggregate and routinely reported country level data. The re-analysis of Bokhari et al. (2007), and Moreno-Serra and Smith (2015) by Nakamura et al. (2016) highlights some of the difficulties including: measurement error (which tends to bias estimates downwards and reduce statistical significance); missing data and the implications of imputation; as well as potentially weak instruments. Better quality and more complete data at country level, as well as finer data at household level, might overcome some of these problems. Estimates based on within country data may be feasible in some LMICs, especially where it is possible to exploit exogenous changes (natural experiments) such as increased public insurance coverage, or where data are available from large scale field experiments which involve changes in health care resources. Whatever the empirical challenges might be, some implicit assessment of health opportunity costs is unavoidable. The range of indicative estimates from Woods et al. (2015) and Ochalek et al. (2015) may provide a useful starting point for its explicit assessment and a process of refinement.

2.4 What are the implications for Malawi?

This evidence suggest that health opportunity costs are likely to be substantially higher (cost per DALY lower) than suggested by global and national bodies that make recommendations about cost-effectiveness (see Section 2.5). This suggests that health care expenditure is more productive and can have a greater impact on health than the implied values and widely cited norms (see Section 2.5). The qualitative implication of this evidence appears to be consistent across all health care systems, but it is especially so for health care systems in low-income countries. Figure 4 expresses the estimates of cost per DALY as a % of GDP pc for all low income countries. It suggests that a cost per DALY that reflects the likely health opportunity costs is almost certain to be lower than 50% of GDP pc and probably significantly lower.

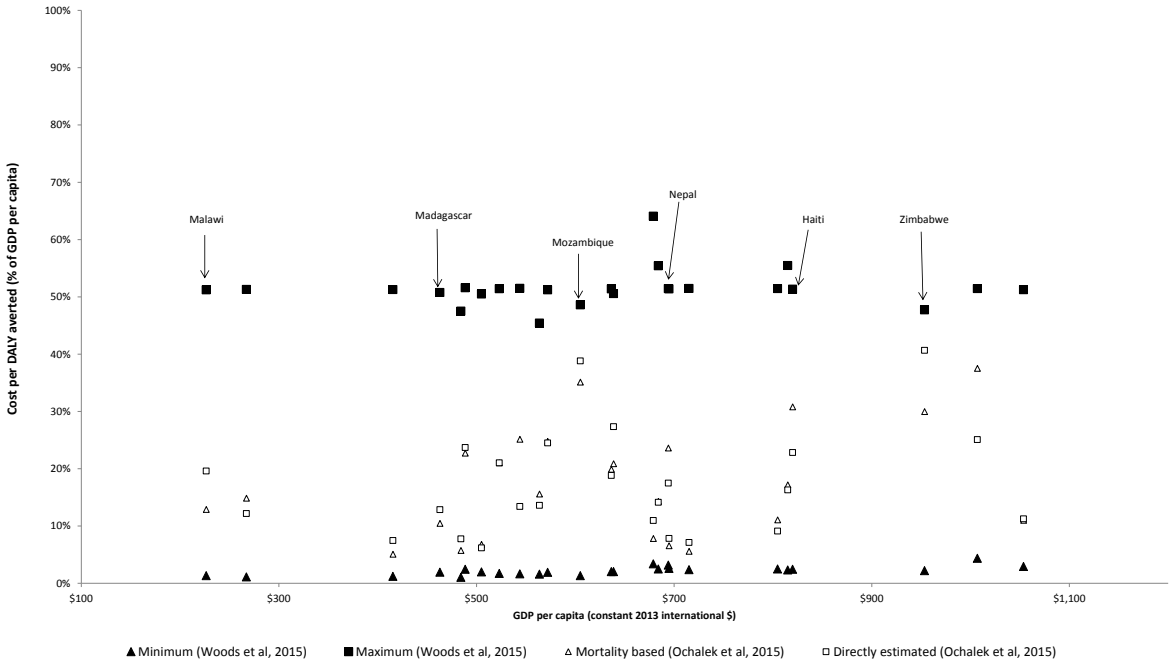


Figure 4 Cost per DALY ranges as % GDP pc for low-income countries

For the reasons set out in Section 2.3 the estimates from Ochalek et al. (2015) may be regarded as the most plausible, because they use more of the evidence that is currently available including: the effects of health expenditure (elasticities) while taking account of country specific measures of infrastructure, donor funding, population (age and gender), mortality rates (age and gender), conditional life expectancies (age and gender) and total health care expenditure. Although the re-estimated elasticities based on Bokhari et al. (2007) represent one of the better approaches to statistical estimation, there are over 60 other published papers in this area; some of which estimate smaller effects (in part because some do not account for endogeneity). A recent but unpublished meta-regression suggests that elasticities might be lower if account is taken of all these other published papers. On the other hand, the effects of aggregation (due to using country level data and all-cause mortality) are likely to underestimate the effects. On balance, we believe it would be best to regard the upper bound from Ochalek et al. (2015) as a plausible lower bound for health opportunity cost in Malawi and the upper bound from Woods et al. (2015) as an extreme upper bound (see Table 2).

Table 2 Estimates of health opportunity costs for Malawi

	Lower estimate		**Upper estimate**	
	$ per DALY	% GDP pc	$ per DALY	% GDP pc
Woods et al. (2015)	$3	1%	$116	51%
Ochalek et al. (2015)	$24	11%	$37	16%

The range of cost per DALY estimates reported in Table 2 that represent health opportunity costs in Malawi can be used to consider which programmes and interventions might be included in an EHP, what the scale of the EHP might be and how efforts to implement interventions might be prioritised. It also allows the health opportunity costs of the other constraints that decision makers face (including restrictions placed on assistance by donors) to be identified. These assessments can be used to prioritise aspects of health care system strengthening and negotiate more effectively with donors on how their assistance can best meet Malawi's health care needs.

An assessment of health opportunity costs that represents what a health care system could have delivered with more or less resources (i.e. the supply side estimate of the marginal productivity of the health care system) is required whether or not there are explicit administrative health care budgets and whether or not there are restrictions on the growth in health expenditure. It is also a key question when considering whether more resources should be devoted to health care. It is not possible to consider sensibly how much should be spent on an activity without some assessment of what is likely to be gained from that expenditure. In the context of health care that requires an assessment of the health effects of health care expenditure, i.e. an assessment of health opportunity costs that represents what a health care system could have delivered with more or less resources. For example, the estimates of health opportunity costs in Table 2 indicate what the current evidence suggests Malawi is currently paying to avert a DALY. When this is combined with information about the health programmes and interventions that are available this also indicates the possible scale (total budget) of the EHP (see Section 3). This estimate might be regarded as too low if many Malawians would wish to pay more to avert a DALY. Higher estimates, such as $60 or $116 per DALY, imply an expanded EHP with a larger budget. Once the health that is likely to be delivered by greater health care expenditure is set out it then becomes possible to have a more meaningful deliberation about how Malawi's public finance resources might be allocated between competing claims (health education, infrastructure etc.) and how increases in public finance might be achieved.

2.5 Other suggested thresholds

Much of the published literature and the values recommended or cited by decision making and advisory bodies (both national and supra national), reflect a lack of conceptual clarity about what a cost-effectiveness threshold ought to represent and what type of evidence might inform its assessment (Revill et al., 2014) (Culyer, 2015). This lack of clarity rests on a failure to distinguish clearly three very different notions of what a cost-effectiveness threshold should represent:

i) An assessment of health opportunity costs based on evidence of the health effects of changes in health care expenditure i.e. a measure of the amount of health that a health care system currently delivers with more or less resources (a supply side measure of the marginal productivity of health care expenditure, see Section 2.1 and 2.3 above).

ii) Established norms, whether explicit or implied values, that simply describe how cost-effectiveness is judged and decisions tend to be made (see below).

iii) The value that ought to be placed on improvements in health. Such values reflect a particular view of what constitutes the social value of health. They imply what the demand for health and health care expenditure ought to be, rather than an evidence based assessment of the health effects of changes in actual levels of health care expenditure (see below).

2.5.1 Norms and implied values

An implicit or explicit assessment of health opportunity costs is unavoidable because all decisions about health care imply one. A few health care systems have revealed something about the type of threshold values likely to be used when making decisions (Vallejo-Torres et al., 2016). However, reimbursement agencies in only two health care systems have been explicit about the threshold used to judge cost-effectiveness, although others seem likely to follow[10]. For example, since 2004,

[10] A commission which considered whether Norway should adopt an explicit threshold has recommended research similar to that conducted in the UK. In the meantime an explicit threshold based on a similar analysis to Woods et al. (2015), is to be adopted until a Norwegian within country estimate is available. Informally, Portugal has amended its implicit threshold, which also appears to be based on a similar analysis to Woods et al. (2015). Other HICs (e.g. Spain, Australia and Netherlands) have already commissioned within country research, and Canada is considering federally funded research to estimate health opportunity costs supported by two of its provincial health care systems.

the National Institute for Health and Care Excellence (NICE), which issues guidance to the UK NHS, has published an explicit range for the cost-effectiveness thresholds used in its deliberative decision making process (£20,000 to £30,000 per QALY). Although NICE makes clear that the threshold ought to represent the health consequences of additional NHS costs, this range was founded on the values implied by the decisions it made between 1999 and 2003 (Rawlins and Culyer, 2004). The NICE thresholds are implied values from previous decisions and have been widely recognised for some time (including by NICE) as having little empirical foundation[11]. This range has become an established norm, which is intended to represent how NICE makes its decisions[12] rather than an empirical assessment of the likely health opportunity costs. Other established norms are also evident in published economic evaluations. For example, in the US, threshold of $50,000 to $100,000 per QALY have become increasingly cited but are widely recognised as having little evidential foundation (Neumann, Cohen and Weinstein, 2014).

2.5.2 The value of health

Other suggested thresholds reflect how much consumption should be given up to improve health. They represent a view of what the demand for health and health care expenditure ought to be, rather than an assessment of the health effects of changes in actual health care expenditure, i.e. a 'supply side' assessment of health opportunity costs.

Thresholds that reflect a view of the demand for health have been expressed in two subtly different ways: aspirational ones, which represent a particular view of what value ought to be placed on health improvements and how much resources should be devoted to health care; and those based on evidence of how much consumption individuals are willing to give up to improve their health. There is a large literature which has used stated preferences (hypothetical valuations) to estimate the consumption value or willingness to pay for a QALY. Most estimate how much consumption an individual is willing to give up to improve their own health. A few try to elicit how much individuals believe society should pay to improve health more generally. A wider literature, that extends beyond health, estimates the value of a statistical life, based on how much consumption individuals are willing to give up to reduce their mortality risk. Some studies are based on stated preferences (hypothetical choices) but others identify situations where individuals actually make choices that imply a value, e.g. revealed preferences in the labour market. A cost per QALY or cost per DALY can be derived from these studies by making assumptions about age and gender distribution, conditional life expectancies and quality of life norms.

Recent reviews of this literature (Vallejo-Torres et al. (2016) and Ryen and Svensson (2014)) reveal very wide variation in values, even within countries. However, some patterns do emerge. Reported values are generally lower than the type of GDP pc based thresholds that have become widely used in LMICs, but tend to be higher than available estimates of a 'supply side' assessment of health opportunity costs. This suggests a discrepancy between the demand and supply side of health care systems. For example, if the type of individual preferences expressed in these studies are regarded as an appropriate expression of social value, the difference would indicate that health care from collectively pooled resources is 'underfunded' compared to individual preferences about health and consumption. However, given the difficulties faced in the public financing of health care systems in high income countries as well as LMICs this is what might be expected.

[11] The House of Commons investigation of NICE in 2008 identified that the thresholds used by NICE had little empirical foundation. In response, NICE commissioned Appleby et al. (2009), and asked UK research funders to commission the research that was published in Claxton et al. (2015a).

[12] NICE does not reject technologies with ICERs less than its stated upper bound of £30,000 per QALY. Current evidence suggests that the thresholds implied by NICE decisions are, in fact, much higher (£39,417 to £43,949 per QALY, (Dakin et al., 2014) even when special considerations do not apply.

However, values based on individual preferences about health and consumption reflects a particular, but quite reasonably disputed, view of what might constitute the social value of health (Drummond et al., 2015). Even if this important and difficult question of social value was not disputed, the estimates imply what health expenditure ought to be rather than reflecting the implications of what health expenditure actually is. Since 'demand side' values, especially aspirational ones, are likely to be substantially higher than an assessment of the actual health opportunity costs (the supply side) their use is likely to reduce overall population health and underestimate the real value of devoting more resources to health care (see Section 2.1).

Some agencies have adopted or recommended explicit thresholds informed by these types of 'demand side' estimates. For example, in 2005 the World Health Organization recommended explicit cost per DALY thresholds to serve as a guide alongside WHO-CHOICE. They have been used as generic and internationally applicable criteria to classify interventions as highly cost-effective (less than one GDP pc), cost-effective (less than three GDP pc) or not cost-effective (three GDP pc or higher). They appear to have been based on estimates of the value of a statistical life reported in the Commission on Macroeconomics and Health 2001. Despite the widely recognised shortcomings of these GDP pc based thresholds (Newall, Jit and Hutubessy, 2014) (Marseille et al., 2015), they have nonetheless become established norms, which are widely cited in published economic evaluations, have informed recommendations made by agencies and, in the absence of other country specific estimates, have been commonly used as a criteria to judge cost-effectiveness in LMICs. The current evidence suggests these established norms are aspirational and substantially higher than available estimates of a 'supply side' estimate of health opportunity costs. They also appear to be higher than other 'demand side' values based on individual preferences about health and consumption.

The only agency in an LMIC that has adopted an explicit evidence based country specific threshold is the Health Intervention and Technology Assessment Program (HITAP) in Thailand. HITAP was established in 2007 and adopted threshold based estimates of individual stated preferences about health and consumption. The values were intended to reflect the social value of health in Thailand (Jirawattanapisal et al., 2009). Based on this research, the Health Economic Working Group under the Subcommittee for Development of the National List of Essential Drugs and the Subcommittee for Development of the Health Benefit Package and Service Delivery of the NHSO recommended a threshold of one GDP pc (120,000 THB per QALY). The organisation has continued to evolve and conduct research to inform this issue, raising the threshold to 160,000 THB per QALY in 2013 (Thavorncharoensap et al., 2013) (Nimdet and Ngorsuraches, 2015). These thresholds are country specific and empirically based estimates but represent a social value of health relative to other consumption opportunities rather than a 'supply side' assessment of health opportunity costs, based on evidence of the health effects of changes in actual health care expenditure.

3. Supporting the development of an Essential Health Package for Malawi

3.1 Introduction

The principles that should shape an analytical framework to guide intervention selection for the EHP in Malawi are set out in Section 1, and the rationale for the centrality of health opportunity costs in that framework are considered in Section 2. In this section the framework is developed and illustrated, and its implications for the EHP are considered. As described in Section 1, the framework needs to assess how much Malawi can afford to devote to the EHP given how much it currently spends on improving population health and what this implies for an EHP budget. The framework should prioritise interventions on the basis of the health benefits they offer the Malawian population taking account of health opportunity costs - the health outcomes that could be achieved by the health system more generally. The analytical starting point for the framework should be to reflect realistic implementation rates of each intervention reflecting the supply and demand side constraints that inevitably exist in getting interventions to in-need populations. This provides a means of quantifying implementation gaps and their implications for reductions in population health. This can show the potential benefits of implementation activities relating to specific interventions and of system strengthening more generally. The framework should also offer a means of assessing the impact on population health of the constraints imposed by donors and, as such, provide a means of communicating to donors and other stakeholders about the potential health benefits of relaxing or reconfiguring those constraints.

In developing this framework, a range of evidence is drawn upon. Table 3 provides a brief summary of the key sources of evidence, and more details are available in Appendix 3. The best data currently available has been brought together, but this can be improved upon and extended over time (see Section 4). The main purpose of the report is to show the principles of the analytical framework, how it can guide a range of important policy questions and its implications for the EHP based on currently available evidence.

Table 3 Summary of evidence sources; full data available for 67 interventions

Type of evidence	Sources
Estimates of cost-effectiveness	Papers found through Tufts Cost-Effectiveness Analysis registry and WHO-CHOICE analyses
DALYs averted	Calculated or taken directly from papers found through Tufts Cost-Effectiveness Analysis registry and WHO-CHOICE analyses
Per patient costs (drugs and supplies)	EHP HSSPII midterm costing (CMST; EPI/GAVI; unlisted)
Estimates of realistic coverage levels	Bottleneck analysis from the EHP HSSPII midterm costing v87
Cases (patients)	EHP HSSPII midterm costing (EmOC report; MNH Roadmap; Malaria Indicator Survey; Malaria costing; etc.)
Health opportunity costs	Woods et al., (In press); Ochalek et al. (2015)

EHP – Essential Health Package; HSSPII – Second Health Sector Strategic Plan II; WHO-CHOICE – CHOosing Interventions that are Cost-Effective

3.2 The appropriate scale of the Essential Health Package

The analytical framework starts by considering the scale of the EHP – that is, the appropriate level of financial resources that should be devoted to the package. To address this question it is necessary to know something about what Malawi currently gets from its public health expenditure in terms of health benefits. This indicates how much Malawi is currently able to afford for health care and provides a means of identifying candidate interventions for the EHP that are expected to generate health at a cost that is consistent with what Malawi can afford. The cost of these candidate

interventions provides information on the size of the budget that might reasonably be devoted to the EHP.[13]

As described in Section 2, an empirical estimate of health opportunity costs is central to understanding what Malawi is currently able to afford to devote to public health care. Health opportunity costs are expressed in terms of the rate at which the Malawian health care system is currently able to translate health care expenditure into improving population health. The framework characterises health in terms of disability-adjusted life years (DALYs) averted (Salomon et al., 2012), so health opportunity costs are expressed as the cost per DALY averted in (US $). As discussed in Section 2, the evidence available on health opportunity costs in particular countries remains limited.

Two studies provide initial estimates of health opportunity costs for low- and middle-income countries, together with appropriate ranges of uncertainty. The first uses UK estimates of health opportunity costs which are extrapolated to other jurisdictions based on the relationship between health opportunity costs and the value of health in terms of forgone consumption, and how the latter varies with national income levels (Woods et al., In press). The second uses available cross-country evidence of the impact of health expenditure on mortality and relates this to DALYs averted and how these are impacted by changes in health expenditure for countries with different demography, epidemiology, levels of expenditure on health care, income and other characteristics (Ochalek et al., 2015). These two studies provide a range of estimates of health opportunity costs for Malawi, reflecting alternative estimation methods and assumptions. Woods et al. (In press) estimate this to range between $3 and $116 per DALY averted (1% to 51% of GDP per capita) (Woods et al., In press); and Ochalek et al. (2015) provide estimates ranging from $24 and $37 per DALY averted (11% to 16% of GDP per capita) (Ochalek et al., 2015). For the purposes of describing the framework, an initial estimate of $61 per DALY is employed based on the mean from these two papers inflated to 2016 US$. The implications of varying this estimate for the scale of the EHP are assessed in Section 3.6.

This starting estimate of health opportunity costs enables an assessment of what interventions are affordable for the EHP. Those interventions that available evidence suggests can generate health at a cost that is less than the health opportunity costs are worthy of consideration. In other words, if the estimated cost per DALY averted for an intervention is less than the cost at which the Malawi health system is able to avert DALYs (initially set at $61 per DALY averted), this is consistent with maximising the impact on population health given financial resource constraints. To pay more than $61 per DALY averted for interventions in the EHP would be inappropriate as resources could be reallocated to the health system more generally and generate greater health outcomes. Similarly, confining the EHP only to interventions with costs per DALY of, for example, $30 per DALY averted and below, would also not make sense as more could be spent on EHP interventions which improve population health when allowing for opportunity costs.

Table 4 shows the key characteristics of the 67 candidate interventions for which evidence is currently available. The interventions are ranked in terms of their incremental cost-effectiveness ratios (ICERs) expressed as expected cost per DALY averted. This is also shown in terms of the number of DALYs averted per $1000 spend [(1/ICER) x $1000]. The table also shows, for each intervention; the estimated number of cases per annum, the total cost per annum, total cumulative cost per annum, and total DALYs averted. On the basis of an estimated health opportunity cost of $61 per DALY averted, the first 48 interventions in Table 4 can be afforded and, together, these

[13] Costs are drug and supply costs. Further information is given in Appendix 3.

would cost $264.5 million per annum which can be considered an appropriate budget for the EHP.[14] The affordable interventions and implied budget are also shown in Figure 5 which plots the DALYs averted per $1000 against cumulative annual expenditure, again assuming 100% implementation.

[14] We assume interventions are independent. In reality, however, there may be complementarities between treatments, and the ICERs could change depending upon which other interventions are provided as part of the package.

Table 4 Prioritising interventions by effectiveness cost

Ranking based on ICER	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost (Malawi cost * patient #s)	Cumulative cost	Total DALYs averted
1	Cotrimoxazole for children	cost saving		127,265	$219,803	$219,803	318
2	Mass media	1	903	6,879,044	$7,608,778	$7,828,581	150,390
3	Isoniazid Preventive Therapy for children in contact with TB patients	1	900	2,227	$7,321	$7,835,902	45,175
4	Isoniazid Preventive Therapy for HIV+ no TB	1	887	55,132	$79,518	$7,915,420	1,118,463
5	First line treatment for new TB cases for adults	3	393	14,465	$178,018	$8,093,438	1,045,196
6	First line treatment for retreatment TB cases for adults	3	393	1,808	$99,632	$8,193,071	130,651
7	First line treatment for new TB cases for children	3	393	12,285	$116,948	$8,310,019	887,697
8	First line treatment for retreatment TB cases for children	3	393	1,536	$65,831	$8,375,850	110,963
9	Clean practices and immediate essential newborn care (home)	3	368	671,464	$415,687	$8,791,536	237,281
10	Case management of MDR TB cases	3	297	70	$12,249	$8,803,786	5,182
11	Malaria treatment: uncomplicated (adult, <36 kg)	4	260	4,371,692	$3,463,077	$12,266,863	59,209
12	Malaria treatment: uncomplicated (adult, >36 kg)	4	260	4,371,692	$4,267,184	$16,534,046	59,209
13	Malaria treatment: uncomplicated - 2nd line (adult, >36 kg)	4	260	4,371,692	$1,186,063	$17,720,109	59,209
14	Malaria treatment: uncomplicated - 2nd line (adult, <36 kg)	4	260	4,371,692	$593,031	$18,313,141	59,209
15	Malaria treatment: uncomplicated (children, <15 kg)	4	260	1,042,154	$4,576,454	$22,889,595	14,115
16	Malaria treatment: uncomplicated (children, >15 kg)	4	260	1,042,154	$4,768,246	$27,657,841	14,115

Ranking based on ICER	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost (Malawi cost * patient #s)	Cumulative cost	Total DALYs averted
17	Malaria treatment: uncomplicated - 2nd line (children, <15 kg)	4	260	1,042,154	$35,322	$27,693,163	14,115
18	Malaria treatment: uncomplicated - 2nd line (children, >15 kg)	4	260	1,042,154	$70,685	$27,763,848	14,115
19	Malaria treatment: First trimester – uncomplicated	5	198	304,921	$1,025,093	$28,788,941	108,854
20	Malaria treatment: Second trimester – uncomplicated	5	198	304,921	$235,320	$29,024,261	108,854
21	Malaria treatment: Pregnant women – complicated	5	198	15,613	$139,592	$29,163,853	5,574
22	Rotavirus vaccine	6	177	650,553	$3,096,648	$32,260,501	88,364
23	Management of pre-eclampsia (Magnesium sulphate)	6	168	20,022	$45,439	$32,305,940	534,719
24	Tetanus toxoid (pregnant women)	7	149	918,437	$114,545	$32,420,485	103,602
25	Vitamin A supplementation in pregnant women	7	140	123,989	$125,197	$32,545,682	33,420
26	Measles vaccine	9	106	650,553	$527,904	$33,073,586	106,659
27	PMTCT	11	94	52,791	$600,432	$33,674,018	157,074
28	Labour and delivery management	11	89	918,437	$1,281,436	$34,955,454	170,442
29	Caesarean section (with complication)	12	86	5,051	$171,925	$35,127,380	137,341
30	Management of obstructed labour	12	86	91,844	$1,099,805	$36,227,184	2,497,118
31	Vaginal delivery, skilled attendance	12	83	918,437	$5,180,964	$41,408,148	66,840
32	Vaginal delivery, with complication	12	83	137,766	$803,890	$42,212,038	10,026
33	Households owning at least one ITN/LLIN	13	77	6,751,618	$13,736,789	$55,948,828	228,063

Ranking based on ICER	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost (Malawi cost * patient #s)	Cumulative cost	Total DALYs averted
34	Pregnant women sleeping under an ITN	13	77	1,469,499	$2,989,832	$58,938,660	49,638
35	Under five children who slept under ITN/LLIN	13	77	494,267	$1,005,632	$59,944,292	16,696
36	Antenatal care (4 visits)	15	68	918,437	$11,230,144	$71,174,436	90,020
37	Blood safety	15	66	39,554	$1,625,986	$72,800,422	11,866
38	Male circumcision	22	45	4,073,429	$146,729,553	$219,529,975	39,634,464
39	Newborn sepsis - Full supportive care	24	42	80,576	$417,192	$219,947,167	60,156
40	Antenatal corticosteroids for preterm labour	25	40	165,319	$405,568	$220,352,735	47,064
41	Voluntary counselling and testing	25	40	8,030,614	$36,308,732	$256,661,467	167,100
42	Schistosomiasis mass drug administration	29	35	388,695	$76,527	$256,737,995	23,754
43	Caesarean section	32	31	33,982	$671,704	$257,409,698	327,465
44	Maternal sepsis case management	39	26	64,291	$2,730,718	$260,140,417	20,052
45	Antibiotics for pPRoM	40	25	64,291	$38,796	$260,179,213	29,509
46	Management of severe malnutrition (children)	50	20	50,790	$2,436,858	$262,616,071	198,831
47	Interventions focused on female sex workers	51	20	23,478	$655,072	$263,271,144	161,351
48	Interventions focused on men who have sex with men	51	20	33,758	$1,255,745	$264,526,889	231,996
49	High cholesterol	68	15	222,947	$6,702,709	$271,229,598	921
50	Basic psychosocial support, advice, and follow-up, plus anti-epileptic medication	82	12	506,371	$1,265,925	$272,495,523	689
51	Zinc (diarrhoea treatment)	99	10	7,455,177	$1,787,880	$274,283,403	244,080

Ranking based on ICER	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost (Malawi cost * patient #s)	Cumulative cost	Total DALYs averted
52	IPT (pregnant women)	110	9	734,750	$34,712	$274,318,115	99
53	Condoms	127	8	8,030,614	$22,882,530	$297,200,645	481,837
54	ORS	153	7	8,661,655	$937,089	$298,137,734	147,171
55	Hypertension	159	6	845,659	$1,337,730	$299,475,465	44,495
56	Treatment of depression	265	4	168,790	$331,621	$299,807,086	115
57	Diabetes, Type I	296	3	23,063	$4,303,914	$304,111,000	25
58	Diabetes, Type II	296	3	138,381	$4,210,622	$308,321,621	149
59	ART for men	312	3	331,746	$21,159,060	$329,480,681	1,005,291
60	ART for women	312	3	508,622	$32,440,372	$361,921,053	1,541,279
61	Ischemic heart disease	453	2	128,130	$4,193	$361,925,246	7
62	Treatment of bipolar disorder	557	2	523,250	$10,361,966	$372,287,212	182
63	GIT, Intestine cancer	804	1	156	$2,711	$372,289,923	0
64	Paediatric ART	892	1	106,677	$7,657,310	$379,947,233	1,556,424
65	Cervical cancer (first line)	1,087	1	2,477	$161,625	$380,108,858	1
66	Treatment of acute psychotic disorders	1,646	1	168,790	$958,081	$381,066,939	27
67	Treatment of schizophrenia	1,646	1	2,363,066	$13,413,129	$394,480,067	376

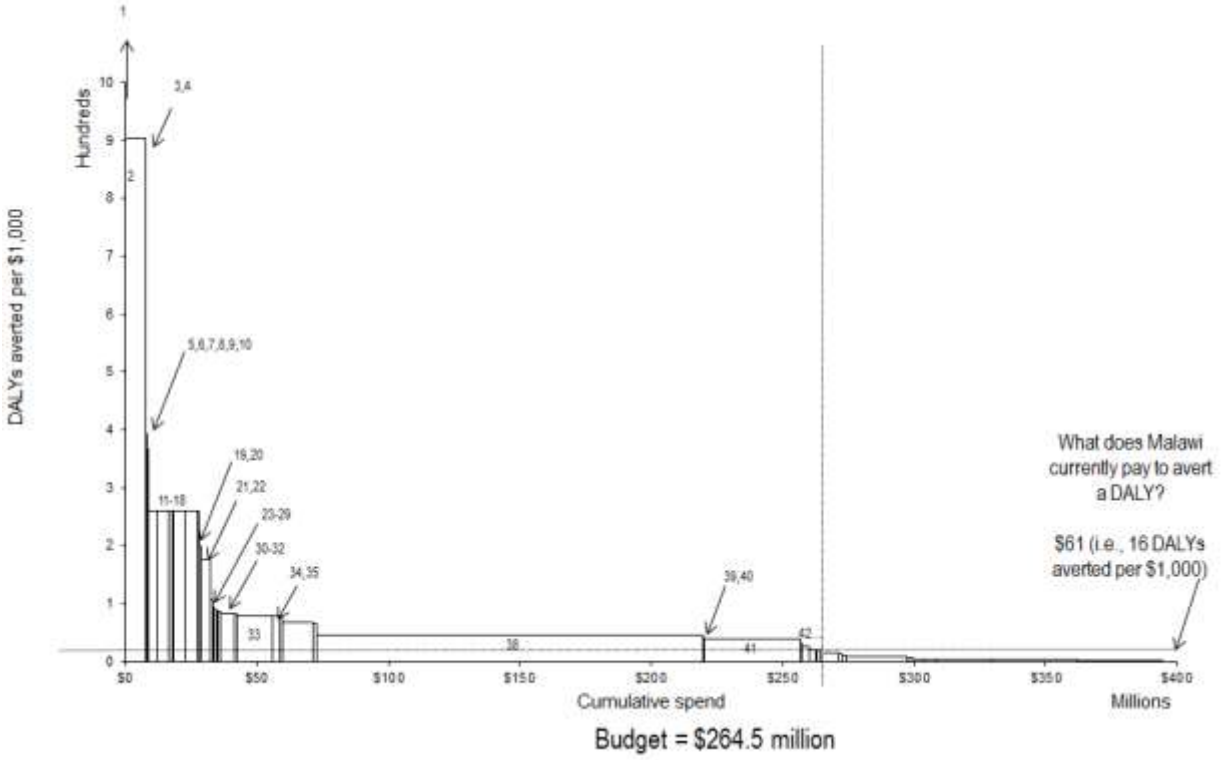


Figure 5 The DALYs averted per $1,000 for EHP interventions that are affordable in Malawi given estimated health opportunity costs of $61 per DALY averted (or 16 DALYs averted per $1,000)

The figure also shows cumulative spend and the implied budget for 100% implementation of each intervention to its relevant target population. The number shown for each intervention relate to the ICER ranking in Table 4.

3.3 Maximising gains in population health from the available budget

Although ICERs are an appropriate way of establishing which interventions are affordable for the EHP given what Malawi currently spends to generate health (here taken as $61 per DALY averted), they cannot be used to prioritise between interventions on the basis of overall gains in population health (i.e. to establish which interventions maximise population health subject to the available budget). This is because prioritising on the basis of ICERs does not consider the size of an intervention's health gain per patient or the number of patients who stand to benefit from the intervention net of the health opportunity cost of the intervention. Table 5 shows the ranking of interventions in terms of overall gains in population health expressed as net DALYs averted assuming 100% intervention implementation for each target population. Net DALYs averted are calculated as follows:

$$D_i - \frac{C_i}{k}$$

Where:

- D_i is the DALYs averted across the relevant population for each intervention i (Column 8 in Table 5).
- C_i is the total annual cost across the relevant population of each intervention i (Column 6 in Table 5)[15].
- k is the health opportunity cost (the cost of averting an additional DALY elsewhere in the health system).

[15] Net DALYs averted are calculated using the same cost as are used to calculate the cost-effectiveness ratios. These are not always equal to the Malawi per patient costs which are presented in column 6 and are used to calculate the size of the package. This is discussed further in Appendix 3.

Several things can be noted from Table 5. Firstly, as expected, the ranking based on net DALYs averted is rather different to that based on ICERs. For example, male circumcision is ranked first compared to its ICER ranking of thirty-eighth, which reflects the fact that it generates a large health impact on its target population which remains higher than other interventions even when health opportunity costs are considered. The second thing to note is that the cost saving intervention ranked first by ICER (i.e. intervention 1) averts fewer net DALYs overall than other interventions which impose costs on the system. This is because the direct health effects of the cost saving intervention plus the opportunity gains (health produced elsewhere from the savings generated by the intervention) are less than those of cost-adding interventions. The third consideration is that those interventions that cannot be afforded by the EHP and were not included in the package in Table 4 and Figure 5 would result in negative overall population health impacts (net DALYs averted) if they had been included. This is because the cost associated with those interventions could be used elsewhere to better effect (i.e. the resources would generate higher DALYs averted than if used for these particular interventions). Figure 6 shows the re-ranking based on net gains in population health, where the latter is compared with cumulative spend. Those interventions that cannot be afforded (beyond the budget of $264.5 million with ICERs above $61 per DALY averted) are shown to generate negative net DALYs averted.

Table 5 Prioritising interventions in terms of impact on overall population health (net DALYs averted)

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost	Cumulative cost	Total DALYs averted	Net DALYs averted (full implementation)
38	Male circumcision	22	45	4,073,429	$146,729,553	$146,729,553	39,634,464	25,423,008
30	Management of obstructed labour	12	86	91,844	$1,099,805	$147,829,358	2,497,118	2,025,734
4	Isoniazid Preventive Therapy for HIV+ no TB	1	887	55,132	$79,518	$147,908,876	1,118,463	1,097,909
5	First line treatment for new TB cases for adults	3	393	14,465	$178,018	$148,086,894	1,045,196	1,001,800
7	First line treatment for new TB cases for children	3	393	12,285	$116,948	$148,203,842	887,697	850,840
23	Management of pre-eclampsia (Magnesium sulphate)	6	168	20,022	$45,439	$148,249,281	534,719	482,789
9	Clean practices and immediate essential newborn care (home)	3	368	671,464	$415,687	$148,664,968	237,281	226,760
33	Households owning at least one ITN/LLIN	13	77	6,751,618	$13,736,789	$162,401,757	228,063	179,981
43	Caesarean section	32	31	33,982	$671,704	$163,073,461	327,465	156,536
2	Mass media	1	903	16,879,044	$7,608,778	$170,682,239	150,390	147,674
28	Labour and delivery management	11	89	918,437	$1,281,436	$171,963,675	170,442	139,385
27	PMTCT	11	94	52,791	$600,432	$172,564,107	157,074	129,751
6	First line treatment for retreatment TB Cases for adults	3	393	1,808	$99,632	$172,663,740	130,651	125,227
29	Caesarean section (with complication)	12	86	5,051	$171,925	$172,835,665	137,341	111,415
8	First line treatment for retreatment TB Cases for children	3	393	1,536	$65,831	$172,901,496	110,963	106,356
19	Malaria treatment: First trimester – uncomplicated	5	198	304,921	$1,025,093	$173,926,589	108,854	99,904

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost	Cumulative cost	Total DALYs averted	Net DALYs averted (full implementation)
20	Malaria treatment: Second trimester – uncomplicated	5	198	304,921	$235,320	$174,161,909	108,854	99,904
41	Voluntary counselling and testing	25	40	8,030,614	$36,308,732	$210,470,641	167,100	98,199
24	Tetanus toxoid (pregnant women)	7	149	918,437	$114,545	$210,585,186	103,602	92,231
26	Measles vaccine	9	106	650,553	$527,904	$211,113,090	106,659	90,230
22	Rotavirus vaccine	6	177	650,553	$3,096,648	$214,209,738	88,364	80,205
36	Antenatal care (4 visits)	15	68	918,437	$11,230,144	$225,439,882	90,020	68,482
11	Malaria treatment: uncomplicated (adult, <36 kg)	4	260	4,371,692	$3,463,077	$228,902,959	59,209	55,503
12	Malaria treatment: uncomplicated (adult, >36 kg)	4	260	4,371,692	$4,267,184	$233,170,142	59,209	55,503
13	Malaria treatment: uncomplicated - 2nd line (adult, >36 kg)	4	260	4,371,692	$1,186,063	$234,356,205	59,209	55,503
14	Malaria treatment: uncomplicated - 2nd line (adult, <36 kg)	4	260	4,371,692	$593,031	$234,949,236	59,209	55,503
31	Vaginal delivery, skilled attendance	12	83	918,437	$5,180,964	$240,130,200	66,840	53,706
3	Isoniazid Preventive Therapy for children in contact with TB patients	1	900	2,227	$7,321	$240,137,521	45,175	44,357
48	Interventions focused on men who have sex with men	51	20	33,758	$1,255,745	$241,393,266	231,996	39,656
34	Pregnant women sleeping under an ITN	13	77	1,469,499	$2,989,832	$244,383,098	49,638	39,173
39	Newborn sepsis - full supportive care	24	42	80,576	$417,192	$244,800,290	60,156	36,567
46	Management of severe malnutrition (children)	50	20	50,790	$2,436,858	$247,237,148	198,831	36,343

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost	Cumulative cost	Total DALYs averted	Net DALYs averted (full implementation)
25	Vitamin A supplementation in pregnant women	7	140	123,989	$125,197	$247,362,345	33,420	29,517
40	Antenatal corticosteroids for preterm labour	25	40	165,319	$405,568	$247,767,913	47,064	28,004
47	Interventions focused on female sex workers	51	20	23,478	$655,072	$248,422,986	161,351	27,581
1	Cotrimoxazole for children	-4,289	0	127,265	$219,803	$248,642,789	318	22,564
15	Malaria treatment: uncomplicated (children, <15 kg)	4	260	1,042,154	$4,576,454	$253,219,243	14,115	13,231
16	Malaria treatment: uncomplicated (children, >15 kg)	4	260	1,042,154	$4,768,246	$257,987,489	14,115	13,231
17	Malaria treatment: uncomplicated - 2nd line (children, <15 kg)	4	260	1,042,154	$35,322	$258,022,811	14,115	13,231
18	Malaria treatment: uncomplicated - 2nd line (children, >15 kg)	4	260	1,042,154	$70,685	$258,093,496	14,115	13,231
35	Under five children who slept under ITN/LLIN	13	77	494,267	$1,005,632	$259,099,129	16,696	13,176
42	Schistosomiasis mass drug administration	29	35	388,695	$76,527	$259,175,656	23,754	12,562
45	Antibiotics for pPRoM	40	25	64,291	$38,796	$259,214,452	29,509	10,473
37	Blood safety	15	66	39,554	$1,625,986	$260,840,439	11,866	8,914
32	Vaginal delivery, with complication	12	83	137,766	$803,890	$261,644,329	10,026	8,056
44	Maternal sepsis case management	39	26	64,291	$2,730,718	$264,375,047	20,052	7,324
21	Malaria treatment: pregnant women – complicated	5	198	15,613	$139,592	$264,514,639	5,574	5,116
10	Case management of MDR TB cases	3	297	70	$12,249	$264,526,889	5,182	4,898
63	GIT, Intestine cancer	804	1	156	$2,711	$264,529,599	0	-0

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost	Cumulative cost	Total DALYs averted	Net DALYs averted (full implementation)
65	Cervical cancer (first line)	1,087	1	2,477	$161,625	$264,691,224	1	-15
61	Ischemic heart disease	453	2	128,130	$4,193	$264,695,417	7	-45
52	IPT (pregnant women)	110	9	734,750	$34,712	$264,730,129	99	-79
57	Diabetes, Type I	296	3	23,063	$4,303,914	$269,034,043	25	-95
49	High cholesterol	68	15	222,947	$6,702,709	$275,736,752	921	-98
50	Basic psychosocial support, advice, and follow-up, plus anti-epileptic medication	82	12	506,371	$1,265,925	$277,002,677	689	-237
56	Treatment of depression	265	4	168,790	$331,621	$277,334,298	115	-382
58	Diabetes, Type II	296	3	138,381	$4,210,622	$281,544,920	149	-568
66	Treatment of acute psychotic disorders	1,646	1	168,790	$958,081	$282,503,000	27	-693
62	Treatment of bipolar disorder	557	2	523,250	$10,361,966	$292,864,966	182	-1,466
67	Treatment of schizophrenia	1,646	1	2,363,066	$13,413,129	$306,278,095	376	-9,704
55	Hypertension	159	6	845,659	$1,337,730	$307,615,825	44,495	-70,870
51	Zinc (diarrhoea treatment)	99	10	7,455,177	$1,787,880	$309,403,705	244,080	-150,097
54	ORS	153	7	8,661,655	$937,089	$310,340,795	147,171	-220,736
53	Condoms	127	8	8,030,614	$22,882,530	$333,223,325	481,837	-517,166
59	ART for men	312	3	331,746	$21,159,060	$354,382,385	1,005,291	-4,103,927

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Total cost	Cumulative cost	Total DALYs averted	Net DALYs averted (full implementation)
60	ART for women	312	3	508,622	$32,440,372	$386,822,757	1,541,279	-6,292,006
64	Paediatric ART	892	1	106,677	$7,657,310	$394,480,067	1,556,424	-21,073,939

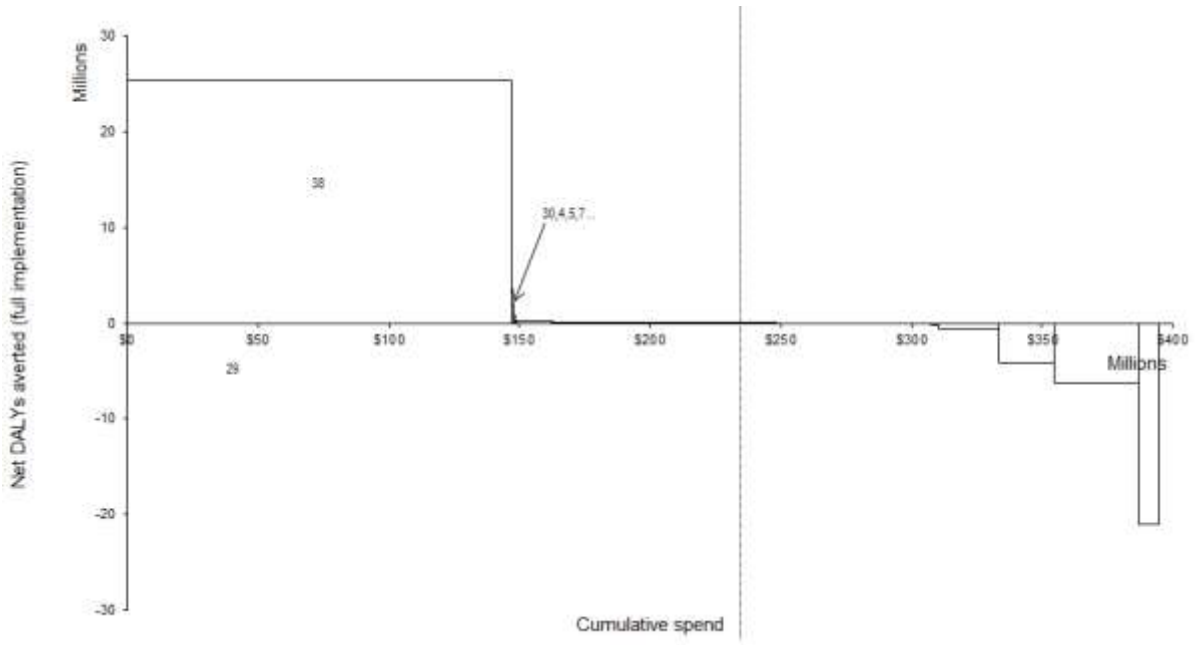


Figure 6 Interventions ranked by net DALYs averted, also showing cumulative spend (assuming 100% implementation)

Shows negative net DALYs averted associated with interventions that cannot be afforded in the package.

3.4 Maximising gains in population health from the available budget

3.4.1 Health effects of less than 100% implementation

So far it has been assumed that each intervention included in the EHP on the basis of affordability is delivered to 100% of its target population. The reality is, however, implementation rarely, if ever, reaches this level. As discussed in Sections 1 and 2 with examples, this reflects a range of possible constraints that operate in health systems, which can be particularly acute in low-income settings. Some of these relate to the demand side – patients failing to take up or to adhere to interventions– and some to the supply side – challenges in getting services to patients. Some of these constraints are specific to particular interventions, and others apply across interventions and relate to the health care system's weaknesses more generally.

The analytical framework that has been developed provides a means of quantifying the impact on population health of this range of intervention-specific and system-level constraints. This is shown diagrammatically in Figure 7 which looks at those interventions included in the EHP (based on Tables 4 and 5) at a budget of $264.5 million. As before, the figure shows the overall impact on population health (net of health opportunity costs) in terms of net DALYs averted, and the cumulative spend across the package. The solid lines show what happens to these metrics when interventions achieve 100% implementation. The dotted lines indicate how net DALYs averted decline as implementation levels fall; the dotted line also shows the underspend on the EHP budget as fewer patients from the target populations receive the relevant interventions.

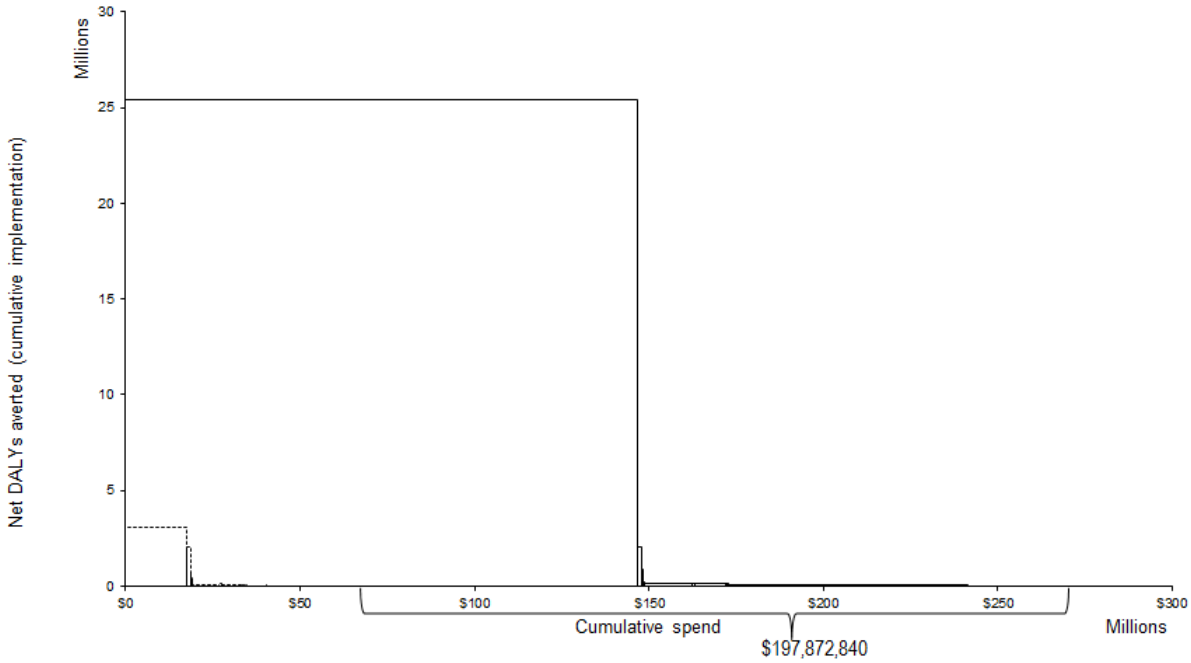


Figure 7 Interventions ranked by net DALYs averted, also showing cumulative spend

Compares full (100% implementation) [solid lines] with lower (<100% implementation) [dotted lines]. Shows impact of limited implementation on net DALYs averted and the budget underspend.

More detail is provided in Table 6 that shows the key metrics with full and partial implementation – spending levels on the intervention (and cumulatively across interventions), DALYs averted and net DALYs averted. The partial levels of implementation are based on what is considered realistic in the Malawi setting and are from a bottleneck analysis from the EHP HSSPII midterm costing (v87). The table also shows the impact of the 'implementation gap' on net DALYs averted. For example, a realistic implementation level for first line treatment of TB in children is 64%. This will generate 850,840 net DALYs averted under full implementation, but only 544,538 at the lower level of implementation, resulting in a net loss to overall population health of 306,303 DALYs averted. The table also shows the magnitude of the budget underspend associated with partial implementation, both at an intervention level and cumulatively across the package. Overall the cumulative cost under partial implementation is $66.7 million from a budget of $264.5 million (underspend of $197.9 million). The information in Table 6 provides useful insights for policy makers considering how to respond to partial implementation of EHP interventions. The framework provides a coherent means of bringing together resource allocation decisions relating to specific interventions funded through the EHP and those relating to implementation and system strengthening.

Table 6 Impact on overall population health (net DALYs averted) and cumulative spend of interventions included in the EHP with 100% implementation and expected (realistic) levels of implementation

#	Intervention	ICER [$]	Pop DALYs averted per 1,000	Cases per annum	Implem' level	Total cost (full implem') [$]	Cumulative cost (full implem') [$]	Total cost (realistic implem') [$]	Cumulative cost (realistic implem') [$]	Total DALYs averted (full implem')	Total DALYs averted (realistic implem')	Net DALYs averted (full implem')	Net DALYs averted (realistic implem')	Difference in net DALYs averted	$ value to the health care system of implem'
38	Male circumcision	22	45	4,073,429	12%	146,729,553	146,729,553	17,607,546	17,607,546	39,634,464	4,756,136	25,423,008	3,050,761	22,372,247	1,372,313,607
4	Isoniazid Preventive Therapy for HIV+ no TB	1	887	55,132	50%	79,518	146,809,071	39,759	17,647,305	1,118,463	559,231	1,097,909	548,955	548,955	33,672,879
5	First line treatment for new TB Cases for adults	3	393	14,465	64%	178,018	146,987,089	113,932	17,761,237	1,045,196	668,925	1,001,800	641,152	360,648	22,122,152
7	First line treatment for new TB Cases for children	3	393	12,285	64%	116,948	147,104,037	74,847	17,836,084	887,697	568,126	850,840	544,538	306,303	18,788,597
9	Clean practices and immediate essential newborn care (home)	3	368	671,464	0%	415,687	147,519,724	0	17,836,084	237,281	0	226,760	0	226,760	13,909,438
23	Management of pre-eclampsia (Magnesium sulphate)	6	168	20,022	80%	45,439	147,565,163	36,351	17,872,435	534,719	427,775	482,789	386,231	96,558	5,922,852
41	Voluntary counselling and testing	25	40	8,030,614	15%	36,308,732	183,873,895	5,446,310	23,318,745	167,100	25,065	98,199	14,730	83,469	5,119,998
22	Rotavirus vaccine	6	177	650,553	0%	3,096,648	186,970,543	0	23,318,745	88,364	0	80,205	0	80,205	4,919,790
33	Households owning at least one ITN/LLIN	13	77	6,751,618	56%	13,736,789	200,707,333	7,706,339	31,025,084	228,063	127,944	179,981	100,969	79,012	4,846,582
19	Malaria treatment: First trimester - uncomplicated	5	198	304,921	33%	1,025,093	201,732,426	341,356	31,366,440	108,854	36,248	99,904	33,268	66,636	4,087,451
27	PMTCT	11	94	52,791	55%	600,432	202,332,858	331,814	31,698,253	157,074	86,803	129,751	71,704	58,047	3,560,625

#	Intervention	ICER [$]	Pop DALYs averted per 1,000	Cases per annum	Implem' level	Total cost (full implem') [$]	Cumulative cost (full implem') [$]	Total cost (realistic implem') [$]	Cumulative cost (realistic implem') [$]	Total DALYs averted (full implem')	Total DALYs averted (realistic implem')	Net DALYs averted (full implem')	Net DALYs averted (realistic implem')	Difference in net DALYs averted	$ value to the health care system of implem'
13	Malaria treatment: uncomplicated - 2nd line (adult, >36 kg)	4	260	4,371,692	2%	1,186,063	203,518,921	17,791	31,716,044	59,209	888	55,503	833	54,671	3,353,500
14	Malaria treatment: uncomplicated - 2nd line (adult, <36 kg)	4	260	4,371,692	4%	593,031	204,111,952	20,756	31,736,800	59,209	2,072	55,503	1,943	53,561	3,285,409
28	Labour and delivery management	11	89	918,437	65%	1,281,436	205,393,388	832,934	32,569,734	170,442	110,787	139,385	90,601	48,785	2,992,465
6	First line treatment for retreatment TB cases for adults	3	393	1,808	65%	99,632	205,493,021	64,761	32,634,495	130,651	84,923	125,227	81,397	43,829	2,688,491
2	Mass media	1	903	16,879,044	71%	7,608,778	213,101,799	5,402,232	38,036,727	150,390	106,777	147,674	104,849	42,826	2,626,920
11	Malaria treatment: uncomplicated (adult, <36 kg)	4	260	4,371,692	30%	3,463,077	216,564,876	1,038,923	39,075,651	59,209	17,763	55,503	16,651	38,852	2,383,198
48	Interventions focused on men who have sex with men	51	20	33,758	5%	1,255,745	217,820,621	62,787	39,138,438	231,996	11,600	39,656	1,983	37,673	2,310,888
36	Antenatal care (4 visits)	15	68	918,437	46%	11,230,144	229,050,765	5,109,715	44,248,153	90,020	40,959	68,482	31,159	37,323	2,289,380
8	First line treatment for retreatment TB cases for children	3	393	1,536	65%	65,831	229,116,596	42,790	44,290,944	110,963	72,126	106,356	69,131	37,224	2,283,350
20	Malaria treatment: Second trimester - uncomplicated	5	198	304,921	67%	235,320	229,351,915	156,723	44,447,666	108,854	72,497	99,904	66,536	33,368	2,046,790
40	Antenatal corticosteroids for preterm labour	25	40	165,319	0%	405,568	229,757,483	0	44,447,666	47,064	0	28,004	0	28,004	1,717,752
39	Newborn sepsis - Full supportive care	24	42	80,576	40%	417,192	230,174,675	166,877	44,614,543	60,156	24,062	36,567	14,627	21,940	1,345,802

#	Intervention	ICER [$]	Pop DALYs averted per 1,000	Cases per annum	Implem' level	Total cost (full implem') [$]	Cumulative cost (full implem') [$]	Total cost (realistic implem') [$]	Cumulative cost (realistic implem') [$]	Total DALYs averted (full implem')	Total DALYs averted (realistic implem')	Net DALYs averted (full implem')	Net DALYs averted (realistic implem')	Difference in net DALYs averted	$ value to the health care system of implem'
1	Cotrimoxazole for children	cost saving		127,265	13%	219,803	230,394,478	27,927	44,642,470	318	40	22,564	2,867	19,698	1,208,247
47	Interventions focused on female sex workers	51	20	23,478	30%	655,072	231,049,551	196,522	44,838,992	161,351	48,405	27,581	8,274	19,306	1,184,254
31	Vaginal delivery, skilled attendance	12	83	918,437	65%	5,180,964	236,230,515	3,367,627	48,206,618	66,840	43,446	53,706	34,909	18,797	1,153,016
12	Malaria treatment: uncomplicated (adult, >36 kg)	4	260	4,371,692	70%	4,267,184	240,497,698	2,987,028	51,193,647	59,209	41,446	55,503	38,852	16,651	1,021,371
24	Tetanus toxoid (pregnant women)	7	149	918,437	84%	114,545	240,612,243	96,218	51,289,864	103,602	87,025	92,231	77,474	14,757	905,196
17	Malaria treatment: uncomplicated - 2nd line (children, <15 kg)	4	260	1,042,154	2%	35,322	240,647,565	530	51,290,394	14,115	212	13,231	198	13,033	799,431
18	Malaria treatment: uncomplicated - 2nd line (children, >15 kg)	4	260	1,042,154	4%	70,685	240,718,250	2,474	51,292,868	14,115	494	13,231	463	12,768	783,199
42	Schistosomiasis mass drug administration	29	35	388,695	13%	76,527	240,794,777	9,949	51,302,817	23,754	3,088	12,562	1,633	10,929	670,393
25	Vitamin A supplementation in pregnant women	7	140	123,989	65%	125,197	240,919,974	81,378	51,384,195	33,420	21,723	29,517	19,186	10,331	633,694
16	Malaria treatment: uncomplicated (children, >15 kg)	4	260	1,042,154	40%	4,768,246	245,688,221	1,907,299	53,291,494	14,115	5,646	13,231	5,292	7,939	486,963
45	Antibiotics for pPRoM	40	25	64,291	30%	38,796	245,727,017	11,639	53,303,132	29,509	8,853	10,473	3,142	7,331	449,676
44	Maternal sepsis case management	39	26	64,291	0%	2,730,718	248,457,735	0	53,303,132	20,052	0	7,324	0	7,324	449,255

#	Intervention	ICER [$]	Pop DALYs averted per 1,000	Cases per annum	Implem' level	Total cost (full implem') [$]	Cumulative cost (full implem') [$]	Total cost (realistic implem') [$]	Cumulative cost (realistic implem') [$]	Total DALYs averted (full implem')	Total DALYs averted (realistic implem')	Net DALYs averted (full implem')	Net DALYs averted (realistic implem')	Difference in net DALYs averted	$ value to the health care system of implem'
46	Management of severe malnutrition (children)	50	20	50,790	80%	2,436,858	250,894,594	1,949,487	55,252,619	198,831	159,065	36,343	29,074	7,269	445,853
3	Isoniazid Preventive Therapy for children in contact with TB patients	1	900	2,227	85%	7,321	250,901,915	6,223	55,258,842	45,175	38,398	44,357	37,703	6,654	408,127
15	Malaria treatment: uncomplicated (children, <15 kg)	4	260	1,042,154	60%	4,576,454	255,478,369	2,745,873	58,004,714	14,115	8,469	13,231	7,939	5,292	324,642
32	Vaginal delivery, with complication	12	83	137,766	51%	803,890	256,282,259	409,984	58,414,698	10,026	5,113	8,056	4,109	3,947	242,133
26	Measles vaccine	9	106	650,553	99%	527,904	256,810,163	522,625	58,937,323	106,659	105,593	90,230	89,328	902	55,347
30	Management of obstructed labour	12	86	91,844	100%	1,099,805	257,909,968	1,099,805	60,037,128	2,497,118	2,497,118	2,025,734	2,025,734	0	0
43	Caesarean section	32	31	33,982	100%	671,704	258,581,671	671,704	60,708,831	327,465	327,465	156,536	156,536	0	0
29	Caesarean section (with complication)	12	86	5,051	100%	171,925	258,753,597	171,925	60,880,757	137,341	137,341	111,415	111,415	0	0
34	Pregnant women sleeping under an ITN	13	77	1,469,499	100%	2,989,832	261,743,428	2,989,832	63,870,589	49,638	49,638	39,173	39,173	0	0
35	Under five children who slept under ITN/LLIN	13	77	494,267	100%	1,005,632	262,749,061	1,005,632	64,876,221	16,696	16,696	13,176	13,176	0	0
37	Blood safety	15	66	39,554	100%	1,625,986	264,375,047	1,625,986	66,502,207	11,866	11,866	8,914	8,914	0	0
21	Malaria treatment: pregnant women - complicated	5	198	15,613	100%	139,592	264,514,639	139,592	66,641,799	5,574	5,574	5,116	5,116	0	0
10	Case management of MDR TB cases	3	297	70	100%	12,249	264,526,889	12,249	66,654,049	5,182	5,182	4,898	4,898	0	0

3.4.2 Prioritising intervention-specific implementation activities

A range of policy options exist to address the constraints facing specific interventions that result in implementation below 100%. These could relate to the demand side (e.g. initiatives to address patients' lack of uptake or adherence to a given intervention) or supply side (e.g. investment in staff training to ensure an intervention is delivered appropriately). Policy makers are unlikely to be able to initiate implementation-enhancing activities for all interventions with partial implementation, and prioritisation will be necessary. Prioritisation of such activities by intervention is informed by the magnitude of loss in population health net of health opportunity cost (net DALYs averted) shown in Table 6. Those interventions with the biggest losses in net DALYs averted as a result of their implementation gaps are the ones with the greatest *potential* benefits from implementation activities because such activities have scope to remove the losses. It is important to emphasise '*potential*', as the implementation activity would have to remove the implementation gap entirely to achieve these gains in overall health. Nonetheless, although best evidence on the effectiveness and cost of the implementation activity would need to be considered (in order to estimate actual gains in overall population health), this provides an initial indication of where a policy to enhance implementation might be prioritised.

Table 6 also shows how much the Malawian health care system might devote to intervention-specific implementation activities; it shows the maximum value, in monetary terms, of policies that remove the implementation gap for each intervention. In other words, this is the maximum the health system should spend on those activities given health opportunity cost (i.e. given the DALYs averted that could be achieved from other activities in the system). It is important to emphasise that these values relate to the whole health system and may not be affordable solely from the EHP budget of $264.5 million.

This is illustrated further in Figure 8 which shows the overall health impact (additional net DALYs averted) associated with eliminating the implementation gap (i.e. taking implementation to 100%) with different levels of expenditure on intervention-specific implementation activities. Each function relates to a specific intervention as would be realistically implemented at the rates shown in Table 6 (i.e. less than 100%). Where a function cuts the horizontal axis, this shows a level of expenditure to remove the implementation gap that is equal to the maximum monetary value to the health care system of implementation. If the system were to devote this amount to implementation-enhancing activities it would not generate any overall health gain (precisely zero additional net DALYs averted on the vertical axis) because this is the maximum value the system can afford. Any more expenditure than this would result in negative net DALYs averted, as shown with the function moving below the horizontal axis with higher levels of implementation expenditure. The net DALYs averted with zero expenditure shows how much overall health can be achieved (gains in net DALYs averted) from removing the implementation gap when the implementation activities cost nothing. This might be the case, for example, if these activities are funded from outside the health care system. This is the same as the maximum overall health benefit that can be achieved from implementation, equivalent to the loss in net DALYs averted shown in Table 6. The slope of each line is the same in the figure, reflecting the rate at which the health system is able to transform financial resources into DALYs averted (assumed $61 per DALY averted here). All that varies between the interventions, therefore, is the maximum value of implementation activities in health terms or monetary terms.

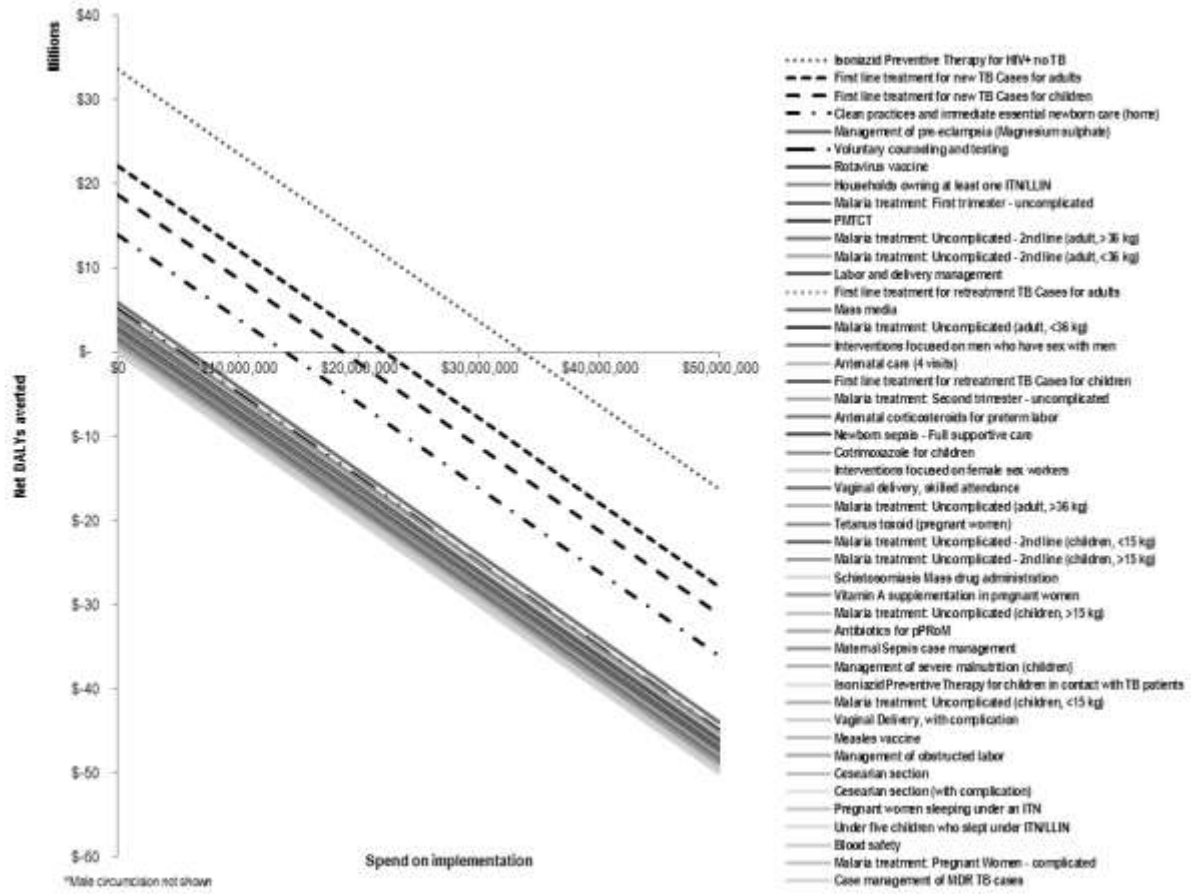


Figure 8 Net DALYs averted at different investment levels for intervention-specific implementation activities for those interventions in the EHP

3.4.3 System-level constraints and system strengthening

Some constraints may relate to specific interventions, but others may impact on the implementation of several or all interventions. There may be scope for system strengthening policies that impact on these system-level constraints. Such policies might include, on the demand side, providing better transport facilities to get patients to health care facilities; on the supply side they may include providing more secure electricity and water supplies. The framework provides an indication of the maximum potential value of system strengthening and can support decisions regarding whether such policies should be prioritised over intervention-specific activities. Given an existing budget for the EHP of $264.5 million, the maximum potential value in health terms of system strengthening would be the additional DALYs averted by removing the implementation gap across all interventions – i.e. the aggregate of additional DALYs averted across interventions. Aggregating the total DALYs averted at 100% implementation across the interventions in the package in Table 6 (49.5 million) and subtracting the total DALYs averted under expected (realistic) levels of implementation (11.4 million) gives the loss in averted QALYs from partial implementation. This is equivalent to the maximum that system strengthening could achieve in health terms if it removed the implementation gaps for all interventions (38.0 million DALYs averted).

This maximum potential gain from system strengthening can be considered alongside the underspend on the budget due to partial implementation discussed above ($197.9 million), which could be used for implementation activities and system strengthening. In principle, the entire underspend could be used on system strengthening activities. However, as this would exhaust the EHP budget, there would be nothing remaining to spend on actually delivering the existing interventions to additional in-need patients. In other words, although longer-term health benefits may be realised from a stronger health system, there would be no immediate health gain (additional

DALYs averted) if the entire EHP underspend was devoted to system strengthening because this would not impact on direct patient care. However, if system strengthening was funded partly or wholly from outside of the health care sector (e.g. by donors and/or central government), then all or part of the underspend on the EHP budget could be devoted to direct funding of existing interventions for which additional implementation is made feasible by the system strengthening.

This is illustrated in Figure 9 which plots DALYs averted against total expenditure on the EHP with a budget of $264.5 million. Two points are plotted. Point A shows the DALYs averted when the system strengthening activities are funded from outside the Malawian health system. This allows the entire underspend to be devoted to delivering the interventions within the stronger system. Assuming system strengthening is able to remove the implementation gap entirely for all interventions, the EHP can achieve DALYs averted from full implementation (49.5 million). Point B shows the point where the entire underspend in the EHP due to partial implementation is devoted to system strengthening. This means that no funding remains to deliver the interventions to additional patients. This results in the aggregate DALYs averted from existing partial levels of implementation (11.4 million). Of course some mix of these two positions is possible: some of the underspend is used to fund system strengthening and the remainder is available to pay for increased delivery of the existing interventions to some level above what is estimated to be realistic levels of implementation, exploiting the stronger system. This would achieve a higher level of DALYs averted than Point B, but lower than Point A. Where it is possible for the EHP to locate between these points will depend on (i) the amount of funding for system strengthening that is available from outside of the health care system; and (ii) the extent to which system strengthening allows the system to increase the implementation of specific interventions.

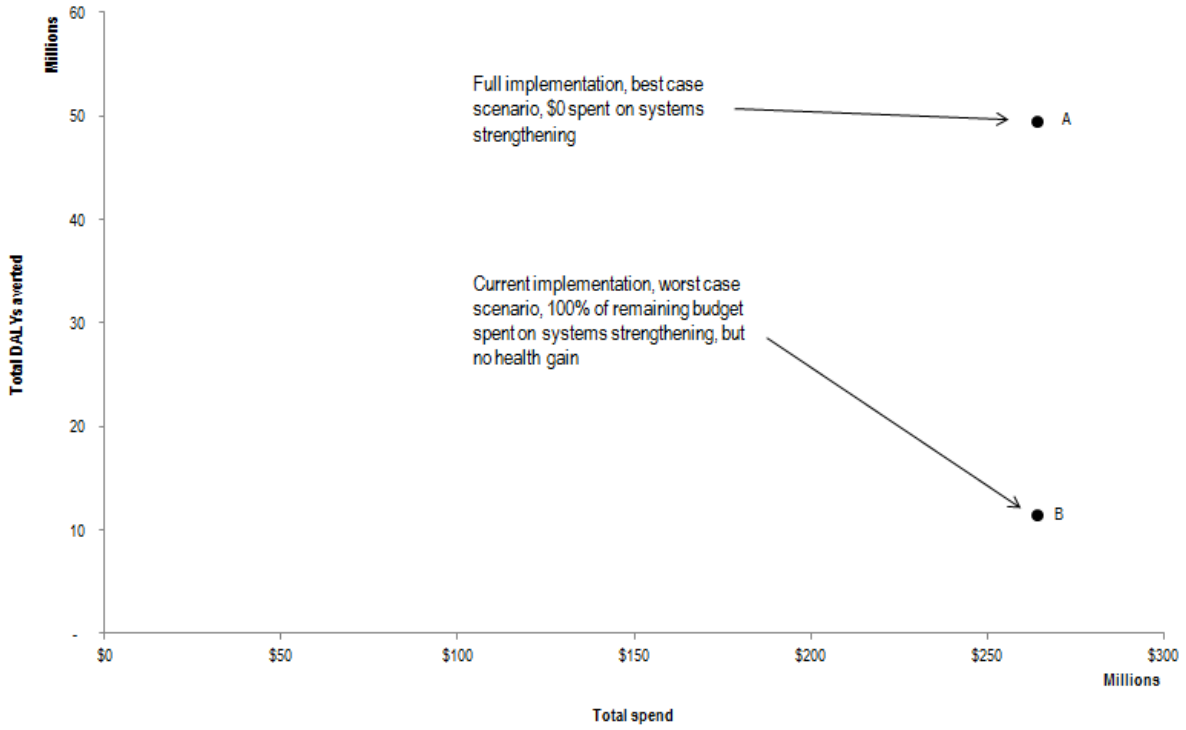


Figure 9 The value of health system strengthening in terms of DALYs averted depending on what proportion of the underspend in the total EHP budget of $264.5 million is devoted to system strengthening versus intervention delivery

Shows two points: A where system strengthening is funded from entirely outside the health system, and B where the underspend is devoted entirely to system strengthening.

3.4.4 Accepting realistic levels of implementation and funding additional interventions

Rather than using the underspend on the EHP budget due to partial implementation of existing interventions on implementation activities and system strengthening, it could be devoted to extending the package. That is, to accept the intervention- and system-level constraints and the resulting partial implementation of interventions, and to use the budget underspend to fund the inclusion of additional interventions that were initially excluded as they had cost per DALY averted estimates greater than $61. This is shown in Table 7 which indicates that the budget underspend ($197.9 million) could be used to include interventions 49 to 67 (see Table 4), in each case implemented at realistic levels (potentially less than 100%). This would generate 14.2 million DALYs averted across the whole expanded package, up to an additional 2.7 million compared to the original package of partially implemented interventions. It should be noted, however, that expanding the package may impact on the implementation levels of currently provided interventions, and as such, this is likely an overestimate of the true number of DALYs that would be generated.

This is further illustrated in Figure 10 which shows a new point, C, added to the chart in Figure 9. This point corresponds to devoting the entire EHP budget underspend to expanding the package. It contrasts with Point A, where system strengthening is externally funded and removes the entire implementation gap across all interventions, allowing the budget underspend to be used to fund the initial set of interventions up to 100%. Point C also contrasts with Point B where the budget underspend is devoted to system strengthening alone, leaving no budget for taking implementation above the initial levels. These three points represent distinct policy approaches to under-implementation due to intervention- and system-level constraints. In reality, a mix of these approaches is likely. For example, there may be a point on Figure 10 that represents the use of the underspend on a mix of system strengthening and delivering existing interventions to more patients made possible by a stronger system. If that point lies between points C and B, policy makers are likely to be influenced by the fact that it will be delivering fewer DALYs averted than using the underspend to add new interventions to an expanded package, accepting lower implementation and not seeking to address the constraints in the system. It should be noted that it may be the case that using the entire underspend on funding system strengthening would result in no immediate health improvement but there are likely to be longer term effects on the ability of the system to generate greater population health through a stronger health care system.

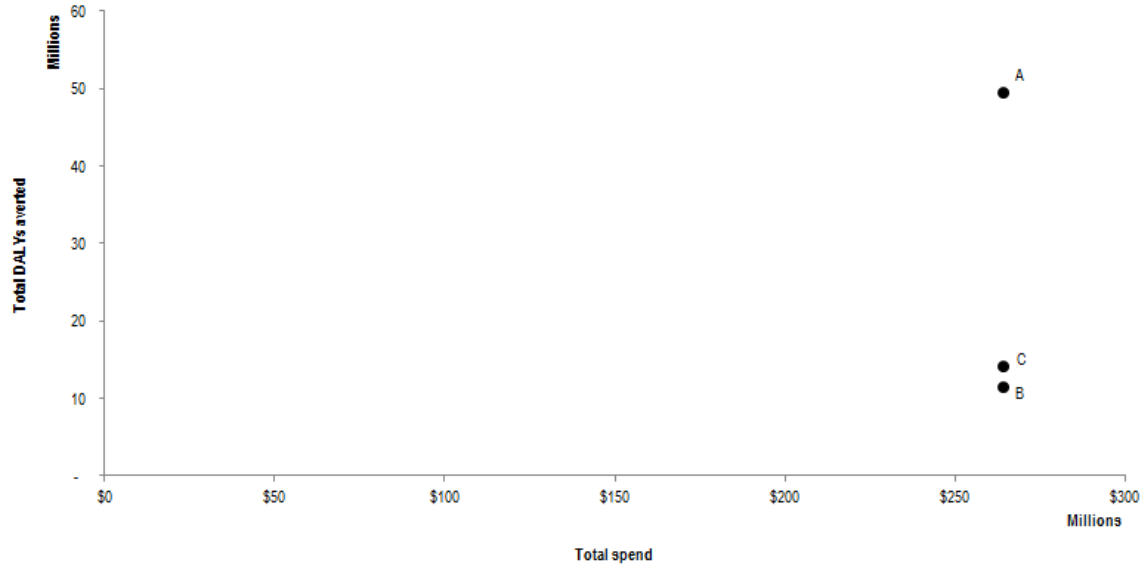


Figure 10 The value of health system strengthening in terms of DALYs averted depending on what proportion of the underspend in the total EHP budget of $197.9 million is devoted to system strengthening versus intervention delivery

The addition of a third point C to those shown in Figure 9 indicates the effects of using the budget underspend on expanding the package.

Table 7 DALYs averted and cumulative costs of additional interventions to the package to allocate the EHP budget underspend due to partial implementation

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Implementation level	Total cost (realistic implementation)	Cumulative cost (realistic implementation)	Total DALYs averted (realistic implementation)
1	Cotrimoxazole for children	cost saving		127,265	13%	$27,927	$27,927	40
2	Mass media	1	903	16,879,044	71%	$5,402,232	$5,430,159	106,777
3	Isoniazid Preventive Therapy for children in contact with TB patients	1	900	2,227	85%	$6,223	$5,436,382	38,398
4	Isoniazid Preventive Therapy for HIV+ no TB	1	887	55,132	50%	$39,759	$5,476,141	559,231
5	First line treatment for new TB cases for adults	3	393	14,465	64%	$113,932	$5,590,073	668,925
6	First line treatment for retreatment TB cases for adults	3	393	1,808	65%	$64,761	$5,654,834	84,923
7	First line treatment for new TB cases for children	3	393	12,285	64%	$74,847	$5,729,681	568,126
8	First line treatment for retreatment TB cases for children	3	393	1,536	65%	$42,790	$5,772,471	72,126
9	Clean practices and immediate essential newborn care (home)	3	368	671,464	0%	$0	$5,772,471	0
10	Case management of MDR TB cases	3	297	70	100%	$12,249	$5,784,720	5,182
11	Malaria treatment: uncomplicated (adult, <36 kg)	4	260	4,371,692	30%	$1,038,923	$6,823,643	17,763
12	Malaria treatment: uncomplicated (adult, >36 kg)	4	260	4,371,692	70%	$2,987,028	$9,810,672	41,446
13	Malaria treatment: uncomplicated - 2nd line (adult, >36 kg)	4	260	4,371,692	2%	$17,791	$9,828,463	888
14	Malaria treatment: uncomplicated - 2nd line (adult, <36 kg)	4	260	4,371,692	4%	$20,756	$9,849,219	2,072
15	Malaria treatment: uncomplicated (children, <15 kg)	4	260	1,042,154	60%	$2,745,873	$12,595,091	8,469

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Implementation level	Total cost (realistic implementation)	Cumulative cost (realistic implementation)	Total DALYs averted (realistic implementation)
16	Malaria treatment: uncomplicated (children, >15 kg)	4	260	1,042,154	40%	$1,907,299	$14,502,390	5,646
17	Malaria treatment: uncomplicated - 2nd line (children, <15 kg)	4	260	1,042,154	2%	$530	$14,502,920	212
18	Malaria treatment: uncomplicated - 2nd line (children, >15 kg)	4	260	1,042,154	4%	$2,474	$14,505,394	494
19	Malaria treatment: First trimester – uncomplicated	5	198	304,921	33%	$341,356	$14,846,750	36,248
20	Malaria treatment: Second trimester – uncomplicated	5	198	304,921	67%	$156,723	$15,003,473	72,497
21	Malaria treatment: pregnant women – complicated	5	198	15,613	100%	$139,592	$15,143,065	5,574
22	Rotavirus vaccine	6	177	650,553	0%	$0	$15,143,065	0
23	Management of pre-eclampsia (Magnesium sulphate)	6	168	20,022	80%	$36,351	$15,179,416	427,775
24	Tetanus toxoid (pregnant women)	7	149	918,437	84%	$96,218	$15,275,634	87,025
25	Vitamin A supplementation in pregnant women	7	140	123,989	65%	$81,378	$15,357,012	21,723
26	Measles vaccine	9	106	650,553	99%	$522,625	$15,879,637	105,593
27	PMTCT	11	94	52,791	55%	$331,814	$16,211,450	86,803
28	Labour and delivery management	11	89	918,437	65%	$832,934	$17,044,384	110,787
29	Caesarean section (with complication)	12	86	5,051	100%	$171,925	$17,216,309	137,341
30	Management of obstructed labour	12	86	91,844	100%	$1,099,805	$18,316,114	2,497,118
31	Vaginal delivery, skilled attendance	12	83	918,437	65%	$3,367,627	$21,683,741	43,446

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Implementation level	Total cost (realistic implementation)	Cumulative cost (realistic implementation)	Total DALYs averted (realistic implementation)
32	Vaginal delivery, with complication	12	83	137,766	51%	$409,984	$22,093,725	5,113
33	Households owning at least one ITN/LLIN	13	77	6,751,618	56%	$7,706,339	$29,800,063	127,944
34	Pregnant women sleeping under an ITN	13	77	1,469,499	100%	$2,989,832	$32,789,895	49,638
35	Under five children who slept under ITN/LLIN	13	77	494,267	100%	$1,005,632	$33,795,528	16,696
36	Antenatal care (4 visits)	15	68	918,437	46%	$5,109,715	$38,905,243	40,959
37	Blood safety	15	66	39,554	100%	$1,625,986	$40,531,229	11,866
38	Male circumcision	22	45	4,073,429	12%	$17,607,546	$58,138,776	4,756,136
39	Newborn sepsis - Full supportive care	24	42	80,576	40%	$166,877	$58,305,652	24,062
40	Antenatal corticosteroids for preterm labour	25	40	165,319	0%	$0	$58,305,652	0
41	Voluntary counselling and testing	25	40	8,030,614	15%	$5,446,310	$63,751,962	25,065
42	Schistosomiasis mass drug administration	29	35	388,695	13%	$9,949	$63,761,911	3,088
43	Caesarean section	32	31	33,982	100%	$671,704	$64,433,614	327,465
44	Maternal sepsis case management	39	26	64,291	0%	$0	$64,433,614	0
45	Antibiotics for pPRoM	40	25	64,291	30%	$11,639	$64,445,253	8,853
46	Management of severe malnutrition (children)	50	20	50,790	80%	$1,949,487	$66,394,740	159,065
47	Interventions focused on female sex workers	51	20	23,478	30%	$196,522	$66,591,262	48,405

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Implementation level	Total cost (realistic implementation)	Cumulative cost (realistic implementation)	Total DALYs averted (realistic implementation)
48	Interventions focused on men who have sex with men	51	20	33,758	5%	$62,787	$66,654,049	11,600
49	High cholesterol	68	15	222,947	1%	$67,027	$66,721,076	9
50	Basic psychosocial support, advice, and follow-up, plus anti-epileptic medication	82	12	506,371	3%	$37,978	$66,759,054	21
51	Zinc (diarrhoea treatment)	99	10	7,455,177	0%	$0	$66,759,054	0
52	IPT (pregnant women)	110	9	734,750	100%	$34,712	$66,793,766	99
53	Condoms	127	8	8,030,614	47%	$10,754,789	$77,548,555	226,463
54	ORS	153	7	8,661,655	69%	$646,592	$78,195,146	101,548
55	Hypertension	159	6	845,659	10%	$133,773	$78,328,919	4,449
56	Treatment of depression	265	4	168,790	1%	$3,316	$78,332,236	1
57	Diabetes, Type I	296	3	23,063	15%	$645,587	$78,977,823	4
58	Diabetes, Type II	296	3	138,381	15%	$631,593	$79,609,416	22
59	ART for men	312	3	331,746	75%	$15,960,590	$95,570,006	758,306
60	ART for women	312	3	508,622	82%	$26,668,904	$122,238,911	1,267,070
61	Ischemic heart disease	453	2	128,130	15%	$629	$122,239,540	1
62	Treatment of bipolar disorder	557	2	523,250	3%	$321,221	$122,560,760	6

#	Intervention	ICER [$]	Population DALYs averted per 1,000	Cases per annum	Implementation level	Total cost (realistic implementation)	Cumulative cost (realistic implementation)	Total DALYs averted (realistic implementation)
63	GIT, Intestine cancer	804	1	156	50%	$1,355	$122,562,116	0
64	Paediatric ART	892	1	106,677	25%	$1,891,657	$124,453,773	384,498
65	Cervical cancer (first line)	1,087	1	2,477	50%	$80,812	$124,534,586	0
66	Treatment of acute psychotic disorders	1,646	1	168,790	1%	$9,581	$124,544,166	0
67	Treatment of schizophrenia	1,646	1	2,363,066	14%	$1,877,838	$126,422,004	53

3.5 Varying the scale of the EHP

The exposition of the framework began by asking what the Malawian health care system is currently able to afford in terms of health-generating activities (health opportunity cost) and using that to identify an appropriate scale for the EHP. This started with an estimate of the cost of averting an additional DALY of $61, an average across a range provided by recent work (Woods et al., In press) (Ochalek et al., 2015), and alternative estimates can be taken from this range. For example, if a lower estimate of $38 per DALY is used to represent what the Malawian health care system is currently able to afford, fewer interventions would be included in the package (interventions 1 to 43 in Table 4), and if a higher estimate is used, $120, more interventions would be affordable within the EHP (interventions 1 to 52 in Table 4).

Exactly the same steps in the framework would be followed for these alternative estimates as previously: prioritising interventions within the EHP on the basis of net DALYs averted allowing for health opportunity cost; assessing the health implications of realistic levels of implementation resulting from intervention- and system-level constraints; prioritising potential intervention-specific implementation activities; assessing the value of system strengthening policies depending on how much of the budget underspend to partial implementation is used as the source of funding; and analysing the extent to which health outcomes would be improved by accepting partial implementation of existing interventions and using the underspend to fund an expansion of the package by adding previously excluded interventions.

This is illustrated in Table 8 which shows, for the EHP budgets implied by the three alternative estimates of affordability (health opportunity cost), total spend and DALYs averted assuming 100% implementation and realistic levels given intervention and system constraints. Table 8 also shows the magnitude of the budget underspend and the health forgone as a result of partial implementation of interventions, with the latter representing the maximum potential gains for implementation activities and system strengthening. The table also shows the health outcomes that can be achieved, under the three alternative EHP budgets, if partial implementation due to constraints was accepted and the budget underspend was used solely to fund additional interventions to an extended package.

Table 8 Three alternative scales of the EHP associated with different estimates of affordability (health opportunity cost) and implications for DALYs averted at full and realistic levels of implementation

	A		B		A-B		C	
	Full implementation		Realistic implementation[16]		Difference between full and realistic implementation		Extended packaged	
How much can Malawi afford to pay to avert a DALY?	Total spend	Total DALYs averted	Total spend	Total DALYs averted	Money left in the budget	Maximum DALYs that could be averted by moving from realistic to full implementa-tion	Total budget	Total DALYs
$38	$ 257,409,698	48,803,384	$ 64,433,614	11,194,346	$ 192,976,084	37,609,037	$ 257,409,698	14,164,820
$61	$ 264,526,889	49,445,122	$ 66,654,049	11,422,269	$ 197,872,840	38,022,853	$ 264,526,889	14,164,820
$120	$ 274,318,115	49,690,912	$ 66,793,766	11,422,398	$ 207,524,349	38,268,514	$ 274,318,115	14,164,820

[16] Estimates of current levels of implementation are provided as part of Appendix 3.

3.6 Assessing the implications of donor-imposed constraints

As discussed in Section 3.5, an important purpose of the framework is to expose the implications for health outcomes and budget underspend of partial implementation due to intervention- and system-level constraints. The framework can also be used to consider the implications of another type of constraint – those imposed by donors. Donors contribute approximately 70% of funding to the Malawian health care system and consequently have considerable influence on resource allocation in the sector. Donors have a range of objectives in the proposals they present to low-income countries, and these will not necessary accord with working with the system to maximise population health subject to internal and donor funding. In principle, donors may be willing to offer the system additional funding which can be used as the system considers appropriate. Using the framework presented here, these additional resources could be devoted to the EHP to fund implementation activities, system strengthening or package expansion, with the objective of maximising health outcomes. However, donors may impose constraints of how, and under what conditions, their additional funding is spent. In negotiating with donors and communicating donor proposals to relevant stakeholders, policy makers will benefit from understanding the implications for population health of such constraints.

To illustrate how the framework can provide this type of information to policy makers, four types of donor constraint are considered: a requirement that a particular intervention is included in the EHP when the money for the intervention could have a bigger impact on health outcomes if spent elsewhere; an offer to expand the package but restricted to a particular intervention when greater health outcomes could be generated by spending elsewhere; an offer to provide additional funding as long as this is matched by the Malawian Ministry of Health and conditional on the funding going on a particular intervention; and an offer to provide additional funding as long as this is matched but without a condition that the funding goes on a particular intervention. The implications of each are considered below assuming a level of affordability reflecting a health opportunity cost of $61 per DALY averted and an implied budget of $264.5 million.

3.6.1 Donor constraint I: forcing interventions into the EHP

To illustrate the implications of the first constraint, it is assumed that a donor proposal has been accepted in the past which has resulted in an intervention being included in the EHP which would not otherwise have been selected on grounds of maximising gains in population health. In other words, by imposing a constraint in return for funding, the donor has effectively forced an intervention into the EHP which resulted in other interventions being excluded which would have delivered greater gains in population health.

To illustrate, assume that the donor's proposal was to provide $4.3 million to the EHP as long as this funding was directed to intervention 57 in Table 4, treatment for Type 1 diabetes. As shown in Table 4 and Figure 5, if the offer of funding had been unconditional, treatment for Type 1 diabetes would not have been included in the EHP. As a result of the constraint, however, the equivalent amount of funding would have had to been taken away from interventions which would have been included under an unconditional funding offer. Assuming interventions generating the least health improvement (least cost-effective) were removed first to make financial space for the diabetes treatment intervention, four interventions would be taken out, as shown in Table 9. These four interventions together, assuming 100% implementation, would have a similar total cost as treatment for Type 1 diabetes ($4.3 million). However, together, those four interventions would result in markedly more DALYs averted: 621,687 compared to 25 with diabetes treatment. This means that the donor constraint resulted in 621,662 fewer DALYs averted than would have been the case if their offer of funding had not been conditional on the resources being devoted to treatment for Type 1 diabetes.

Table 9 Health effects of donor constraints I: forcing an intervention into the EHP

	Interventions cut					Intervention forced in
#	45	46	47	48	45, 56, 47 & 48	50
Intervention	Antibiotics for pPRoM	Management of severe malnutrition (children)	Interventions focused on female sex workers	Interventions focused on men who have sex with men	Total interventions cut	Type 1 Diabetes treatment
Cost	$ 38,796	$ 2,436,858	$ 655,072	$ 1,255,745	$ 4,386,472	$ 4,303,914
DALYs averted	29,509	198,831	161,351	231,996	621,687	25

In providing this type of information, the framework could have offered support to policy makers when the proposal was being considered. In discussion with the donor, the Ministry of Health could have used the information to make clear the opportunity cost – in terms of population health – that was being imposed on Malawi. This may have directed attention to those interventions (e.g. the four listed in Table 9) for which the donor's funding could have been used to greater effect, potentially facilitating some form of negotiation.

3.6.2 Donor constraint II: conditional expansion of the package

The second donor constraint is similar to the first but can be thought of as a new proposal to augment the existing EHP budget, but only if the resources are devoted to a specific intervention. Assume the existing package relates to the $264.5 million and 48 interventions (at 100% implementation) shown in Table 4. The donor proposal is to provide another $4.3 million (taking the total budget to $268.8 million), conditional on those resources being devoted only to a specific new intervention, treatment for Type 1 diabetes, which is not currently in the EHP.

Table 10 shows the implications of this conditional package expansion. As before, devoting $4.3 million of additional funding to treatment for Type 1 diabetes would add 25 DALYs averted. However, if the offer of that additional funding had been unconditional, and the Ministry of Health had been free to use it to expand the package as it saw fit, the additional resources could have been devoted to those interventions generating the greatest additional impact in population health. From the interventions detailed in Table 4, an unconstrained choice of how to spend the additional funding, with the purpose of health maximisation, would have added interventions 50, 51, 52 and 54. This would have resulted in 392,040 DALYs averted, 392,015 more than the intervention imposed by the donor. Hence, the constraint imposed by the donor would result in an opportunity cost, in terms of population health, of 392,015 DALYs averted.

Table 10 Health effects of donor constraints II: conditional expansion of the EHP

#	Other interventions currently not in the EHP						
	50	51	52	54		57	
Intervention	Basic psychosocial support, advice, and follow-up, plus anti-epileptic medication	Zinc (diarrhoea treatment)	IPT (pregnant women)	ORS	Total	Treatment for Type 1 diabetes	Health opportunity cost
Cost	$ 1,265,925	$ 1,787,880	$ 34,712	$ 937,089	$ 4,025,606	$ 4,303,914	
DALYs averted	689	244,080	99	147,171	392,040	25	392,015

As before, the information provided by the framework using available evidence would support decisions about an appropriate policy response to the donor offer. In negotiations with the donor, the Ministry of Health can present the estimates with the aim of working with the donor to use the additional funding for those interventions with the greatest health impact. One explanation for the donor making the additional funding conditional on it being used for a specific intervention is concern that corruption might result in those resources not being used appropriately if the offer was unconditional. The assessment then becomes whether the anticipated loss in DALYs averted due to possible corruption under an unconditional offer is greater than the expected opportunity cost (392,015 DALYs averted) that the framework indicates will be forced on the system by a conditional offer. So the framework provides estimates to frame discussions between the government and donors.

3.6.3 Donor constraint III: Donor matched funding conditional on funding of a particular intervention

The third type of donor offer considered is one where additional funding is offered to augment the EHP budget, but this has to be matched by the Malawi government and the total additional funding needs to be devoted to a specific intervention that is currently not in the EHP, because it does not generate a sufficient gain in health outcomes for its cost (it is not cost-effective). As for the last example, assume that the donor wants to make the proposal conditional on funding going to a particular intervention, treatment for Type 1 diabetes costing $4.3 million. However, now the funder is only willing to fund $2.15 million of this, requiring the remainder to come from the EHP budget. In order to free-up $2.15 million, the Ministry of Health will have to cut interventions and lose the health outcomes they achieve. As before, assume the least cost-effective interventions are removed (i.e. those generating the least DALYs averted from their funding) as necessary to release the $2.15 million. This involves cutting four interventions, with the freed-up funding, together with $2.15 million from the donor, being used to fund treatment of Type 1 diabetes. The new total budget increases to $266.7 million compared to the original $264.5 million but, under the new arrangements, 480,004 fewer DALYs averted are generated, representing the health opportunity cost of the constraint imposed by the donor[17].

3.6.4 Donor constraint IV: Donor matched funding without conditions

It is useful to contrast the proposal in Section 3.6.3 with one where the donor's offer of additional matched funding is not conditional on the extra resources being devoted to a particular intervention not currently in the EHP. In other words, to contrast it with a donor proposal of extra funding which,

[17] If the costs that are used to determine the size of the package are the same as (i.e., from the same source and equal) those that are used to calculate ICERs and net benefit, then forcing programs into the EHP (constraint I) will have a higher health opportunity cost than conditional donor matched funding. This is discussed in Appendix 3. See also footnote 13.

although needing matched funding from the EHP budget, can be used as considered appropriate by the Ministry of Health. Assume the donor is again willing to provide $2.15 million with matched funding from the EHP budget. Given the Ministry's objective of maximising gains in population health, the absence of a condition means no existing interventions need to be removed from those funded by the original budget of $264.5 million. Indeed, the additional $2.15 million from the donor can be used to add interventions to the package from those not currently funded (Table 4), but these can be selected in order to maximise gains in health outcomes from the additional resources. On that basis, it would be possible to add six interventions. From the new effective budget of $266.7 million and with these additional six interventions, total DALYs averted would be 49.4 million.

The costs and health outcomes of these alternative donor offers are contrasted in Table 11. The table shows the total budget and DALYs averted prior to the new donor offer, together with the costs and outcomes of the two matched funding offers. As detailed in the last section, compared to the position pre-offer, the conditional matched funding donor proposal results in a reduction in DALYs averted of 480,004. In contrast, matched funding of the same amount but without the condition of that funding being devoted to a specific intervention (here, Type 1 diabetes treatment), results in an additional 911 DALYs averted compared with the pre-offer position. Therefore, if the donor decides to impose a condition to their matched funding that the resources are devoted to a particular intervention rather than leaving it unconditional, the health opportunity cost is 480,915 DALYs averted.

Table 11 Comparing the implications of two donor proposals with matched additional funding: one unconditional and one conditional on the extra resources being used to fund a specific intervention

	A	B	A-B	C	A-C	**(A-B)-(A-C)**
	Original package (i.e., all resources marshalled and allocated by gov't to maximize population health)	Matched conditional funding scenario	Minimum health opportunity cost of matched conditional funding for Type 1 diabetes treatment	Matched unconditional funding scenario	Health benefit of matched unconditional funding compared to the original package	**Matched conditional versus unconditional funding**
Cost	$ 264,526,889	$ 266,678,846		$ 266,678,846		
DALYs averted	49,445,122	48,965,118	480,004	49,446,033	-911	**480,915**

Again, the magnitude of the impact on population health of imposing a condition is important to be able to communicate to the donor. Of course, the degree of any health opportunity costs will depend on the details of the donor offers, but the analytical framework provides a means of establishing the health impact and can provide an essential support for negotiation. In the context where a donor proposal includes a constraint that imposes considerable health opportunity costs (e.g. the matched conditional funding above), refusal of the offer may be entirely reasonable. The framework's estimates of the health opportunity costs the proposal would have imposed provide a valuable basis for explaining the decision to stakeholders.

3.7 Allowing for additional objectives

The framework presented here shows how the key concept of an empirical estimate of health opportunity costs, together with best evidence on the costs and health effects of potential interventions, can guide decisions about the EHP with an underlying objective of maximising

population health from available resources. Of course there may be a range of other objectives that policy makers wish to factor into their resource allocation decisions and to influence which interventions are included in the package. These objectives might include, for example, enhancing financial protection for vulnerable individuals and reflecting the contribution to net productivity of key groups in the population.

How can the framework support decisions where a more complex set of objectives is operating? It may be the case that considering a wider set of objectives makes no difference to resource allocation: the interventions that offer the greatest impact on population health are also the best available to satisfy other objectives. This may often be the case, for example, when concerns for enhancing productivity are important in selecting interventions for the EHP because, in general, those interventions generating the greatest health outcomes, net of health opportunity costs, give the greatest opportunity for productive activities. This will not always be the case, however, and trade-offs may be necessary – that is, decisions that accept a reduction in aggregate population health in order to achieve one or more additional objectives such as enhancing financial protection. The framework presented here provides a valuable role in informing decisions characterised by trade-offs. This is because it is able to quantify the magnitude of the health opportunity costs associated with a decision to select an intervention to further a wider set of objectives. This provides policy makers with a basis to understand whether that trade-off is worth making and a means of communicating their ultimate decision to stakeholders.

4. Establishing and implementing an Essential Health Package

This section provides some concluding comments on how the framework presented in Section 3 can be used by policy makers and enhanced over time.

4.1 Ongoing use of the framework to inform Essential Health Package decisions

As discussed in Section 1, to date the Malawian EHP has been reassessed every 5 years. Following decisions being made about the 2016 EHP, there is a strong case for a more frequent consideration of the scale of the package, the interventions to be included and the funding of intervention-specific implementation activities and system strengthening. This is because a number of the key considerations in developing the EHP are subject to rapid change over time. The first of these relates to how much the Malawian health care system can afford to devote to EHP; the rate at which it is able to transform available resource into health gains for its population. This is dependent on a range of factors including the total resources available from public finance and donors, the restrictions imposed on that funding (by donors in particular, but perhaps also central government), and the productivity of the health care system (itself a function of the strength of the system).

A second consideration that is subject to change is the availability of new interventions to enhance health outcomes. Additional investment opportunities can come through commercial development of new medical technologies, innovation in the organisation and delivery of health care, and research-based improvements in interventions and the system. A third consideration that is subject to potentially rapid change is the acquisition cost of particular proprietary products as part of interventions (e.g. pharmaceuticals). This can reflect factors such as competition from new market entries, the end of patent protection, and international political pressure. A fourth consideration is rapid development of evidence about the costs and effectiveness of existing interventions, both those in the EHP and those not currently funded. Although much of this evidence is international, it can have relevance to decisions in Malawi.

Creating an ongoing process of updating the EHP that allows decisions to reflect the rapid change in these types of considerations provides the greatest opportunity to maximise the gains in health for the Malawian population.

4.2 Building on available evidence

The framework presented in Section 3 uses best evidence currently available. This evidence relates to the rate at which the Malawian health care system can currently transform financial resources into gains in population health (the health opportunity cost), and to the costs and effects of the range of candidate interventions for the EHP. The first type of evidence is currently limited to two recent pieces of work (Ochalek et al., 2015) (Woods et al., In press) and is subject to uncertainty which should be reflected in how the framework is used (i.e. by employing different scenarios regarding the estimated health opportunity cost as shown in Section 3.5). Ongoing international work to provide estimates of health opportunity costs relevant to individual jurisdictions is central to evidence-based resource allocation decisions, and providing a more precise estimate for Malawi is likely to be a priority research area.

The evidence on the costs and effects of potential EHP interventions used in the framework to date needs further development. Other sources of data are likely to be available shortly (e.g. the WHO's full-sectoral CHOICE analysis for Malawi) and these should be included. Over time the richness of the available data should improve. One aspect of this that will be potentially important is to be able to distinguish the intervention-specific cost of adding an intervention to the package from the cost of those resources that are shared across several interventions. This may be important when, for example, a decision is being considered to remove an intervention from the EHP: some or all of the

former may be released if the intervention is taken out of the package, but the latter will not. Currently that distinction is not possible from the data available.

4.3 Analysis versus decision making

It is important to emphasise that the analytical framework and the results it has generated so far are not dictating a list of interventions to include in the EHP. Rather, this analysis is intended to support a decision making process within the Ministry of Health. This is sometimes referred to as the distinction between assessment (analysis based on available evidence) and appraisal (decision making). Decision making needs to be able to interact with the analytical framework in a number of ways. This includes providing clarity about the scope of decisions that are being addressed – in particular, the balance between selecting interventions for the EHP, making investment decisions for intervention-specific implementation activities and system strengthening, and responding to funding proposals from donors. There is also a key role for decision makers in providing information about a wider set of objectives that might be relevant to decisions other than gains in population health. Decision makers may also have relevant information on intervention- and system-level constraints that might exist and their implications for plausible levels of implementation. Policy makers may also provide valuable input into establishing the best available evidence relating to particular interventions, in particular the cost of delivery.

Appendix 1. Review of the 2011 Essential Health Package

Alongside the introduction of a Sector Wide Approach (SWAp) in the health sector, Malawi introduced its first Essential Health Package (EHP) in 2004. EHP services were to be provided free of charge to patients at government health care facilities as well as some other facilities through agreements. A second EHP was introduced from 2011-2016. It expanded upon the package defined in 2004 to reflect that disease patterns and available resources had changed and to take into account new technologies that had been introduced (Phoya et al., 2010). While the 2004-2010 EHP focused on reducing infant and under five mortality, improving maternal mortality rates, preventing HIV and reducing population growth, the 2011-2016 package recommended gradual expansion to include, for example, 'cost-effective' interventions for non-communicable diseases and a package of 'highly cost-effective' surgical procedures (Ministry of Health, 2012).

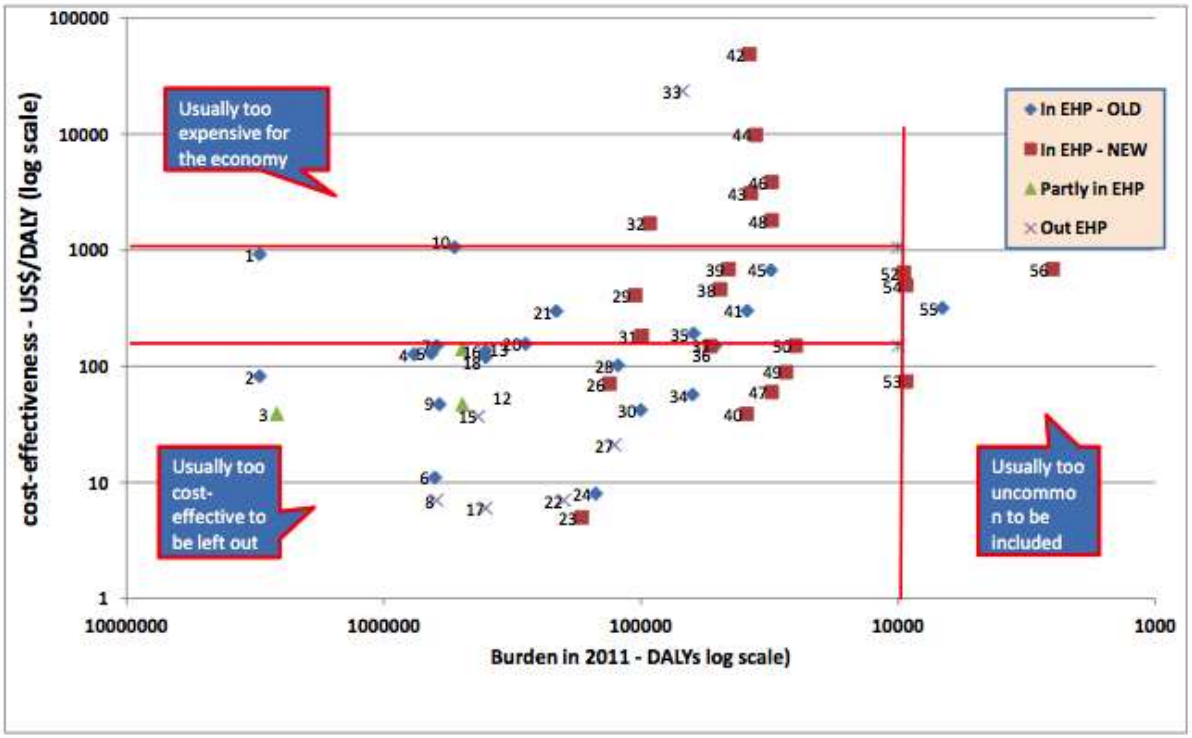
The 2011 EHP was based upon two main criteria: BoD and cost-effectiveness (Phoya et al., 2010). Burden of disease evidence was based upon estimates from the College of Medicine, which updated the 2002 burden of disease estimates for individual countries produced by the World Health Organization (WHO) Global Burden of Disease (GBD) in 2002 and updated in 2004, as well as the STEPS study on non-communicable diseases (Mathers, Boernma and Ma Fat (2008) and Phoya et al. (2010)).

Diseases were ranked by the disability adjusted life years (DALYs) associated with them. Thirteen conditions were named as contributing most heavily to the BoD in Malawi: HIV/AIDS, ARI, malaria, diarrhoeal diseases, perinatal conditions, non-communicable diseases (NCDs), tuberculosis, malnutrition, cancers, vaccine preventable diseases, mental illness and epilepsy, neglected tropical diseases (NTDs), and eye, ear, and skin infections. Nine of these were included in the first EHP that was part of the Program of Work (PoW) 2004-2010; cancers, mental illness and epilepsy, and NTDs being new additions that were also included in the 2011-2016 EHP (Ministry of Health, 2012).

Burden of disease provides a systematic and transparent criterion for resource allocation. Indeed, the scale of the health gains associated with implementing an intervention depend upon the size of the population that would benefit, and burden of disease can be a good proxy measure for this. Although it provides useful information alongside estimates of cost effectiveness, it should not be used as a criterion itself. Burden of disease has implications for the budget, as interventions for diseases with high burden may have large budget impacts, in which case the expected health opportunity costs of a proposed intervention with high budget impact should be estimated using a lower rate of financial resources spent to achieve a unit of health gain, since large budget impacts displace more productive activities. Ultimately, it is the impact of different interventions that needs to be known, not the impact of different diseases (Williams, 1999).

Using burden of disease, 56 interventions were identified and evaluated for cost-effectiveness. Cost-effectiveness estimates were obtained from Disease Control Priorities Second Edition (DCP2), and were not specific to Malawi. Interventions were determined to be cost-effective if they had an ICER at or below $150 per DALY averted. This measure of the opportunity cost of health spending lacks an empirical foundation, and likely represents an overestimate of the effect of spending in the health sector on health outcomes. Using a measure that is too high leads to net losses in population health as the health opportunity costs of interventions are underestimated.

Figure A1 shows the 56 interventions that were considered for the 2011-2016 EHP. The interventions are listed in order of disease burden (e.g. intervention 1 is for HIV/AIDS, which contributes the most to BoD in Malawi) (Bowie and Mwase, 2011).



Legend

1-ARV; 2-HIV prevention; 3-IMCI; 4-Maternal care; 5-ARI in under-5s; 6-Malaria – bednets; 7-Malaria in under 5s using ACT; 8-IPT child; 9-HCT; 10-Dehydration Thanzi; 11-Home made ORS; 12-Water supply; 13-Improved sanitation; 14-Family planning; 15-School health; 16-Wounds, fractures; 17-First aid training of volunteers; 18-Emergency ambulance service; 19-IRS; 20-Management of OIs; 21-Penta vaccine; 22-DPT Polio; 23-NTD mass treatment; 24-Measles vaccine; 25-Supplementary Feeding; 26-Rotavirus vaccine; 27-Prevention of RTAs; 28-Treatment - smear pos. TB; 29-BP - polypill; 30-Growth monitoring; 31-Cataract extraction; 32-Depression; 33-Cancer; 34-STIs; 35-PMTCT; 36-Aspirin for stroke; 37-Malaria in 4-year-olds + ACT; 38-Anxiety disorders; 39-IHD - drugs; 40-Trachoma surgery; 41-Treatment - smear neg. TB; 42-Drug misuse; 43-Bipolar disorders; 44-Schizophrenia; 45-CBHBC; 46-Diabetes - screening; 47-Diabetes - lifestyle change; 48-Diabetes - drugs; 49-Epilepsy; 50-CCF drugs; 51-IPT Preg; 52-Alcohol misuse - PC advice; 53-Cervical screening - cryotherapy; 54-HPV; 55-TB relapsed; 56-Rheumatic h d[42].

Figure A1 Burden of disease and cost-effectiveness of interventions in Malawi (Ministry of Health, 2012)

A number of interventions are cost-effective according to the $150/DALY averted criterion used and have a high burden of disease, but were not included in the package. Technical Working Groups were tasked with appraising the potential interventions and deciding which were included in the package. Practical reasons are given for some of these choices and the authors argue that a rationale exists for all. One example is intermittent prophylaxis for malaria, which although it is cost-effective, it is not yet part of the strategy of the Malaria Unit (Ministry of Health, 2012). (For additional rationales, see DCP3 Working Paper #9.) However, the health opportunity cost of these decisions was not explicitly valued to inform the decision making process.

Although the 2004 and 2011 packages were designed to allocate only the portion of the budget designated to the EHP, the package was estimated to cost 83-132% of total health expenditure (THE). Overestimating the ability of the health care system to pay for the package results in net losses in population health. Interventions are initially financed as if enough resources available, but the budget is eventually exhausted before all the promised interventions are provided in full. As a

result, the budget is spent on a mix of all EHP interventions and not necessarily the most cost-effective ones. Lower health gains than could have been achieved by the budget are actually achieved.

Table A1 Per capita EHP cost and actual health spending

EHP	Year	EHP cost pc	Total Health Expenditure (THE) pc in US$	EHP cost pc as a % of THE pc
1 (2004-2010)	2004	$17.53 (a)	$16.32	107%
1 (2004-2010)	2005	$17.53 (a)	$17.49	100%
1 (2004-2010)	2006	$17.53 (a)	$21.06	83%
1 (2004-2010)	2007	$17.53 (a)	$17.74	99%
1 (2004-2010)	2008	$28.56 (b)	$25.36	113%
1 (2004-2010)	2009		$28.73	
1 (2004-2010)	2010	$44.40 (b)	$33.57	132%
2 (2011-2015)	2011	$44.40 (b)	$38.80	114%
Sources:				
(a) A Joint Programme of Work for a Health Sector Wide Approach (SWAp) 2004 - 2010 (Ministry of Health, 2004).				
(b) Ministry of Health, Malawi				
(c) WHO Global Health Expenditure database (World Health Organization, 2016).				

In summary, the 2011 EHP failed to deliver a package that maximized population health. It put forth two criteria for determining which interventions were included in the package, burden of disease and cost-effectiveness. Neither was perfectly adhered to and ultimately decisions around what to include incorporated additional objectives and were not fully transparent. The use of $150 per DALY for evaluating health opportunity costs is likely to underestimate said opportunity costs and burden of disease is not in itself a criterion under which health will be maximised.

Appendix 2. Measures of cost-effectiveness

The results of economic evaluation are commonly summarised as incremental cost-effectiveness ratios (ICERs), which provide a useful summary of how much additional resource is required to achieve a measured improvement in health (e.g. the additional cost per DALY averted), or how much health is delivered for an amount of additional resource (e.g. the DALYs averted per $1,000). However, to decide whether the intervention will improve health outcomes overall (and should be regarded as cost-effective), a comparison is required with an assessment of the likely health opportunity costs.

A2.1 Problems with cost per DALY measures (one active treatment)

An assessment of health opportunity costs makes it possible to express cost-effectiveness as the expected additional net health or net monetary benefit offered. It indicates the scale of the potential overall impact of ensuring an intervention is fully implemented and identifies the amount of resource that might be devoted to these efforts.

Even when there is only one active treatment, a focus on cost per DALY does not necessarily indicate which programmes ought to be prioritised for implementation efforts because cost per DALY does not indicate the scale of the potential overall impact. The examples of technologies T1 –T4 in Section 2 are reproduced in Table A2. In this example the intervention with the lowest cost per DALY (T4) also offers the greatest value (expressed as net DALY averted or $ value to the health care sector (HCS)) and the intervention with the next highest cost per DALY (T1) offers the lower value.

Table A2 Prioritising implementation efforts (same population)

Technology	ICER ($/DALY)	DALYs averted (,000 DALYs)	HCS Costs	Net DALYS averted (,000 DALYs)	$ Value to HCS
T3	$300	200	$60m	-100	-$20m
T2	$200	200	$40m	0	0
T1	$100	200	$20m	100	$20m
T4	-$100	200	-$20m	300	$60m

However, these examples are a very special case where the health benefit per patient is the same (2 DALYs averted) for each intervention and the population of patients that can benefit from each are also the same (100,000 for each). Even when the per patient health benefit remains the same, any differences in the size of the population that can benefit will mean that cost per DALY measures will not necessarily rank interventions by the value they offer and will not indicate the scale of value (in DALYs or $).

This is illustrated in Table A3 which uses the same interventions (T1-T4) with the same estimate of health opportunity costs ($200 per DALY), the same per patient benefits, and the same total population (400,000). The only difference is that the population that can benefit differs by intervention (T1=300,000, T2=80,000, T3=10,000 and T4=10,000). Intervention T1, which has a higher cost per DALY than T4, offers the greatest value (expressed as net DALY averted or $ value to the HCS). The cost per DALY summary measures are the same in Tables A2 and A3, but the priorities for implementation efforts differ, as does the importance of considering specific constraints. In addition, the amount the HCS might devote to dealing with intervention specific constraints or system weaknesses also differs. Therefore, cost per DALY measures alone cannot be used to prioritise implementation efforts and system strengthening. An assessment of health opportunity costs makes it possible to estimate the scale of the potential impacts on overall health outcomes of implementation efforts in a way that reporting ICERs and categorical judgments about cost-effectiveness cannot.

Table A3 Prioritising implementation efforts (different population)

Technology	ICER ($/DALY)	DALYs averted (,000 DALYs)	HCS Costs	Net DALYS averted (,000 DALYs)	$ Value to HCS
T3	$300	20	$6m	-2	-$10m
T2	$200	160	$32m	0	0
T1	$100	600	$60m	300	$300m
T4	-$100	20	-$2m	30	$10m

A2.2 Problems with cost per DALY measures (multiple alternatives)

When there is more than one active intervention available within a programme (for a specific population with a particular indication) the use of cost per DALY is even more problematic. An assessment of health opportunity costs which enables measures of the net DALYs averted and $ value to HCS overcomes these difficulties.

Informing a decision requires identifying the possible alternative courses of action that could be taken to improve the health of patients who face a choice between mutually exclusive alternatives (i.e. either/or decisions), including not offering active treatment. Often, there is more than one active alternative available (alternatives include the different combinations or sequences of treatment and different ways in which interventions can be used). In these circumstances there are multiple pairwise comparisons that can be made, each providing different incremental costs and DALYs averted, resulting in a number of different cost per DALY ratios that could be reported. This is illustrated in Table A4 and graphically in Figure A2, where there are four alternative active treatment strategies (T1-T4), plus no treatment (T0), for a specific indication and patient population.

Table A4 Multiple alternatives and multiple cost per DALY measures

Alternative interventions	DALYs averted pp	HCS costs pp	Cost per DALY averted compared to:			
			No treatment	Next most effective	Next 'best' (dominance)	Next 'best' (extended dominance)
T0	0	$0	-	-	-	-
T1	1	$100	$100	$100	$100	$100
T2	2	$600	$300	$500	$500	-
T3	3	$1,800	$600	$1,200	-	-
T4	4	$1,000	$250	-$800	$200	$300

These are just some of the pairwise comparison than can be made. The question is which comparisons are appropriate? The comparison should be with the next 'best' (most cost-effective) alternative. Unless comparisons are made with the next best alternative, an intervention might appear worthwhile simply because it has been compared to an alternative which itself is not worthwhile (anything can look good if compared to something sufficiently bad).

For example, T4 appears cost saving when compared to T3, but T3 itself is not worthwhile because it is less effective and more costly than T4 (T3 is strongly dominated; it lies to the north west of T4 in Figure A2). Once T3 is removed from consideration T4 appears just worthwhile when compared to T2 (at a 'threshold' of $200 per DALYs). However, T2 itself is not worthwhile ($500 per DALY compared to T1). In fact, T2 would never be chosen irrespective of which 'threshold' reflected health opportunity costs. For example, at $500 per DALY, T2 would be regarded worthwhile compared to T1 but a decision-maker should not be satisfied with T2 because T3 would offer greater health improvements at a cost per DALY that would also be regarded as worthwhile. Therefore, T2 will never be chosen (it is extendedly dominated). This is also illustrated graphically in Figure A2. Point T2 lies to the north-west of the part of the line that joins T4 and T1. T2 can be thought of as

being strongly dominated by some combination or 'mixture' of T4 and T1. This type of 'mixture' is often not regarded as feasible (e.g. due to equity constraints), so T2 remains extendedly rather than strongly dominated but importantly it will never offer the highest net DALYs averted (see Table A5).

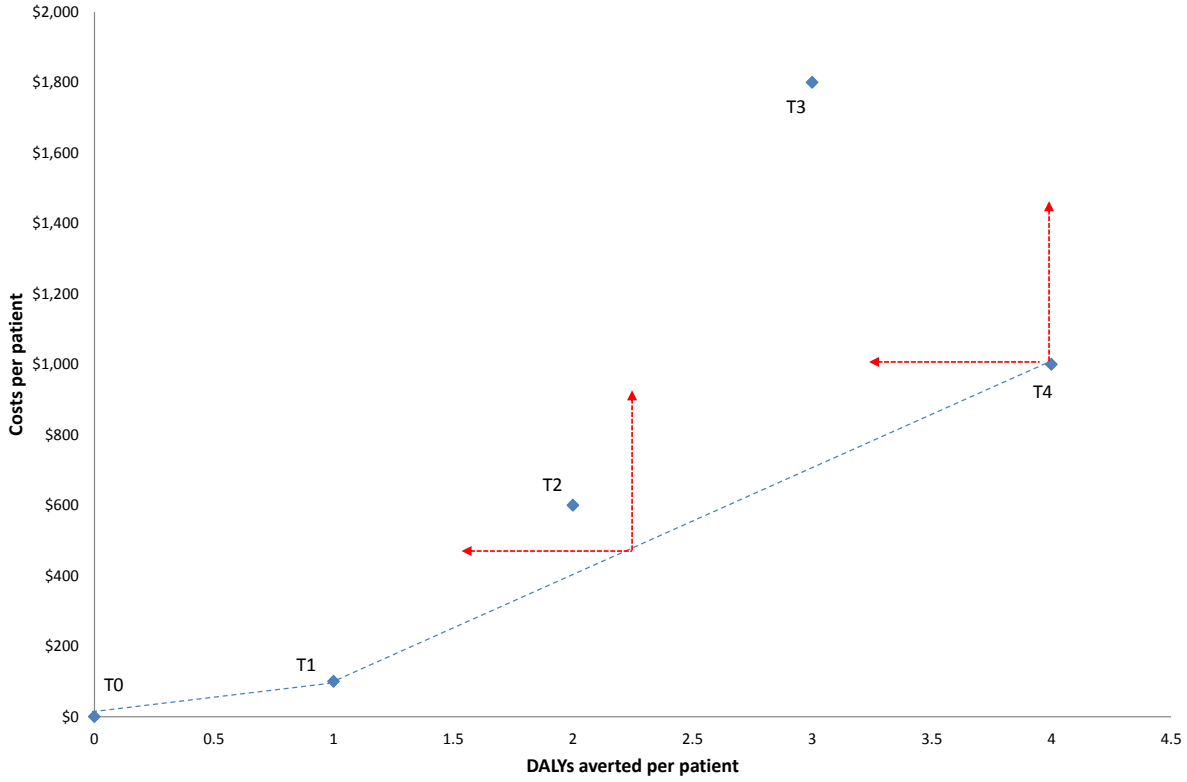


Figure A2 Multiple mutually exclusive alternatives

The difficulties of using ratios based on pairwise comparisons to describe the cost-effectiveness of multiple alternatives can easily be overcome once an assessment of health opportunity costs has been made, because this allows the value of each mutually exclusive alternative to be expressed in terms of net DALY averted or the $ value to the HCS. This is illustrated in Table A5, assuming a population of 100,000 and health opportunity costs of $200 per DALY. It is T1 which offers the highest, and positive, net DALY averted (and $ value of HCS). Therefore, if the HCS was able to afford $200 per DALY, this programme should be covered in an EHP but the intervention included to deliver this programme should be restricted to T1.

Table A5 Choosing between multiple alternatives

Alternative interventions	DALYs averted (,000 DALYs)	HCS costs	Net DALYs averted (,000 DALYs)	$ value to HCS
T0	0	0	0	0
T1	**100**	**$10m**	**50**	**$10m**
T2	200	$60m	-100	-$20m
T3	300	$180m	-600	-$120m
T4	400	$100m	-100	-$20m

In summary:

i) The mutually exclusive alternative intervention which should be included in an EHP is the one with highest value (net DALYs averted or $ value to the HCS).

ii) If T0 (no treatment) is the highest (all others reduce health outcomes overall) then the programme (the collection of mutually exclusive interventions) should not be covered.

iii) There is no need to consider which pairwise comparisons should be made or identify which are strongly or extendedly dominated because they will never offer the highest value (net DALYS or $ value to the HCS).

iv) Whichever pairwise comparison is made when reporting cost per DALY - so long as it is possible to recover the total DALYs averted and the total HCS costs for the target population - then, when combined with an assessment of health opportunity costs, this pairwise comparison can be used to inform which programmes should be covered in an EHP and which interventions within each programme should be included.

Appendix 3. Guide to the living library of data for use in the development of an Essential Health Package

The development of an Essential Health Package (EHP), aligned to the principles set forth in Section 2, requires reliable data. This appendix describes the living library of data created for this purpose and provides a guide to its continued use and maintenance. The appendix is structured in five sections:

1. Data requirements
2. Data used for the development of the 2011 EHP
3. Identification of additional data
4. Data conversion and use
5. Summary of data collected and future use by Ministry of Health and partners

A3.1 Data requirements

The key data needed for each intervention in order to consider it for inclusion within the package are those that enable comparisons of cost-effectiveness and calculation of net benefits. These are:

1. Estimates of cost-effectiveness
2. DALYs averted compared to a 'do nothing' strategy
3. Number of cases (or patients) and realistic coverage levels
4. Per case (or patient) costs

Some of the data are more difficult to obtain than others, but all are necessary to quantify appropriately the health benefits and opportunity costs associated with possible packages that could be provided.

A3.2 Data used for the development of the 2011 Essential Health Package

The process for obtaining data for the 2016 revision of the EHP involved first reviewing the data sources used to develop the 2011 EHP for appropriateness and availability. See Appendix 1 for further details on the review of the 2011 EHP. The 2011 EHP relied on estimates of cost-effectiveness from one source: Disease Control Priorities Project second edition (2006) economic evaluation studies in low- and middle-income countries (DCP2). Although DCP2 provides estimates for a comprehensive list of potential interventions, the underlying cost and DALYs averted are generally not included. As shown in Section 2 estimates of cost-effectiveness alone are an inadequate basis for decision making[18]. Additionally, as DCP2 was published in 2006 and drew upon a number of studies published well prior to this, many studies upon which the estimates were based are now out of date and more recent studies with relevant data were likely to also be available. DCP2 was therefore deemed not to be an appropriate source of estimates for the 2016 EHP revision. DCP is currently being updated in a 3rd edition with more recent cost-effectiveness estimates. If the underlying cost and effectiveness data are also published, this could be a useful source from which to draw upon in future when these are made publicly available.

A3.3 Identification of additional data

The World Health Organization Choosing Interventions that are Cost-Effective (WHO-CHOICE) team was identified as a good candidate for providing the necessary data. The WHO-CHOICE team are currently undertaking comprehensive analyses of the cost-effectiveness of interventions relevant to the new Malawian EHP. However, despite requests made to both DCP and WHO-CHOICE teams, these updated estimates were not made available by the deadline set for the EHP revision.

[18] In the absence of any additional data reliable ICERs would still be better than nothing to form an EHP, but where additional data exists this should be incorporated for better decision making.

Alternative sources of cost-effectiveness were therefore required. The Tufts Global Health Cost-Effectiveness Analysis Registry was identified as a comprehensive database of peer-reviewed studies containing cost-per-disability adjusted life year (DALY) estimates on global health. The database included 484 cost-effectiveness studies applied to low- and middle-income settings. These studies were screened, and those containing estimates relevant to Africa and, where there were multiple studies of the same interventions, the more recent and/or those more applicable to Malawi were prioritised. The database included 16 WHO-CHOICE studies published since 2005 and 26 other studies, resulting in 42 studies that were reviewed in depth. This was supplemented by systematic review of the cost effectiveness of vaccines that was also found, and for which the original studies in the bibliography were reviewed.

The review of cost-effectiveness studies was undertaken under very tight time and resource constraints. It was pragmatic and was neither exhaustive nor systematic. The framework for the EHP should continue to be populated on an ongoing basis by the Ministry of Health and partners to ensure the choice of interventions reflects best available international evidence on the cost-effectiveness as it can be applied to the Malawian context. The establishment of processes and systems to ensure this occurs is the responsibility of the Ministry of Health and its core partners.

A3.4 Data conversion and use

From the papers, identified data on items 1-4 listed above was extracted. Further detail about how these data were converted for use the development of the 2016 EHP are given below.

A3.4.1 Estimates of cost-effectiveness

The constituent parts of the cost-effectiveness ratio are costs and DALYs averted. (See Appendix 2 for further discussion of methods.) In order to compare cost-effectiveness ratios it is necessary that they are in the same currency. Estimates of cost-effectiveness from the papers were reported in various currencies (e.g. 2000 Int$, 2008 US$, etc.). Where costs were given in Int$ these were first converted into US$ using the appropriate years' PPP exchange rate for Malawi provided by the World Bank and then inflated to 2016 US$ using inflation rates from US Inflation Calculator[19]. Table A6 provides the rates used. The cost-effectiveness ratios were then recalculated using the 2016 US$ cost and the DALYs averted as reported by the original source. Due to the currency conversion applied to the numerator of the ratio, many of the cost-effectiveness ratios used in this report are not the same as those reported by the study from which they are drawn, but instead reflect current costs estimated to be incurred in Malawi. It is assumed that evidence on clinical effectiveness generalises to Malawi. This facilities comparability of cost-effectiveness studies and enables estimation of net benefits in the Malawian context.

Ideally, estimates of cost-effectiveness would be specific to Malawi using both costs and DALYs averted from studies in Malawi. This is discussed in more detail in Section 3.5.

[19] World Bank PPP conversion rates: http://data.worldbank.org/indicator/PA.NUS.PPP; US Inflation Calculator: http://www.usinflationcalculator.com/

Table A6 Currency conversion rates

Malawi 2000 PPP conversion factor	**0.223**
Cumulative inflation (year to 2016)	
2000	0.395
2001	0.357
2002	0.335
2003	0.306
2004	0.272
2005	0.230
2006	0.192
2007	0.159
2008	0.116
2009	0.120
2010	0.102
2011	0.068
2012	0.046
2013	0.031
2014	0.015
2015	0.014

A3.4.2 DALYs averted compared to a 'do nothing' strategy

Data on DALYs averted per patient for each intervention were used directly from papers where these were provided. In other cases, DALYs averted were estimated using additional data from the paper (e.g. patient population, per patient costs and cost effectiveness ratios). See Berry et al (2010), Roberts et al (2016), Vassall et al (2014) and Wilford et al (2012) in Table A7.

WHO-CHOICE papers typically give cost-effectiveness estimates for World Health Organization regions. To move from the estimate of DALYs averted in the region to DALYs averted per year in Malawi the following additional data was required:

- pop_R population of the region (i.e. AFR-E or AFR-D)
- pop_M population of Malawi
- pop_{M_D} population of patients in Malawi with disease D
- P population of Malawi as a proportion of the population of the region (i.e., pop_{Malawi}/pop_r)

The data used on the population from the region and the population of Malawi was from the World Bank[20]. The estimates of the Malawi patient population for conditions were obtained from the Palladium Group and Clinton Health Access Initiative (CHAI) Malawi country office, for which assistance is greatly appreciated. Table A7 lists the format of the data and how it was converted for use in the development of the EHP for each source from which data was collected.

[20] World Bank population data: http://data.worldbank.org/indicator/SP.POP.TOTL

Table A7 Data sources

Source	Costs as given by source C_S	Currency	DALYs averted as given by source D_S	Region R	Method for calculating costs for Malawi C_M	Method for calculating DALYs averted for Malawi
Adam et al. (2005)	Yearly costs in millions	2000 Int$	Yearly DALYs averted (millions)	AFR-E	$C_M = C_S * P * million$	$D_M = D_S * P * million$
Alistar et al. (2014)	Per patient costs	2014 US$	Per patient QALYs	South Africa	$C_M = C_S * million / pop_{South\ Africa}$	$D_M = D_S * million / pop_{South\ Africa}$
Baltussen et al. (2012)	Yearly costs in millions for 62,000 patients	2000 Int$	Yearly DALYs averted (millions) for 62,000 patients	AFR-E	$C_M = C_S * \frac{million}{62{,}000} * pop_{M_D}$	$D_M = D_S * \frac{million}{62{,}000} * pop_{M_D}$
Berry et al. (2010)	Net cost using GAVI alliance prices (Intervention cost – Treatment cost) for a birth cohort of 582,211	2008 US$	Total DALYs averted for a birth cohort of 582,211	Malawi	$C_M = C_S$	$D_M = D_S$
Ciaranello et al. (2015)	Discounted per patient lifetime costs (3%)	2013 US$	Discounted per patient lifetime DALYs averted (3%)	Zimbabwe	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Chisholme et al. (2012)	Annual cost per million population in millions	2000 Int$	Annual effect (DALYs saved) per million population	AFR-E	$C_M = C_S * pop_R * P$	$D_M = D_S * pop_R * P/million$
Darmstadt et al. (2005)	Millions	2000 Int$	DALYs averted (millions)	AFR-D	$C_M = C_S * million * \frac{pop_M}{pop_R}$	$D_M = D_S * million * \frac{pop_M}{pop_R}$
Morel et al. (2005) (online)	Cost per year in millions per one million population [i.e. cost per capita]	2000 Int$	DALYs averted per year per one million population	AFR-E	$C_M = C_S * pop_M$	$D_M = D_S * pop_M/million$
Creese et al. (2002)	Unit cost	2000 US$	Effectiveness, DALYs gained per unit	Kenya, Tanzania	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Gaziano et al. (2014)	1. Appx cost per patient 2. Total cost	2012 US$	Total DALYs averted	South Africa	$C_M = C_{S1} * pop_{M_D}$	$D_M = \frac{C_{S1}}{C_{S2}} * D_S * pop_{M_D}$
Hogan et al. (2005)	Yearly costs in millions	2000 Int$	Yearly DALYs averted (millions)	AFR-E	$C_M = C_S * P * million$	$D_M = D_S * P * million$
Kapoor et al. (2016)	Net cost per individual	2014 US$	DALYs per individual	India	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$

Source	Costs as given by source C_S	Currency	DALYs averted as given by source D_S	Region R	Method for calculating costs for Malawi C_M	Method for calculating DALYs averted for Malawi
Lo et al. (2015)	1. Appx cost per patient 2. Total cost	2014 US$	Total DALYs averted	Cote D'Ivoire	$C_M = C_S * pop_{M_D}$	$D_M = \frac{C_{S1}}{C_{S2}} * D_S * pop_{M_D}$
Revill et al. (2015)	Cost saving per patient year	2013 US$	DALYs averted per patient year	Uganda, Zimbabwe	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Robberstadt et al. (2004)	Per patient	2001 US$	Per patient	Tanzania	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Roberts et al. (2016) – emergency caesarean	Not provided, calculated as ICER*DALYs averted	2012 US$	Total DALYs averted for 196 patients	Zambia	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Roberts et al. (2016) – elective caesarean	Not provided, calculated as ICER*DALYs averted	2012 US$	Total DALYs averted for 11 patients	Zambia	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Tan-Torres Edejer. et al (2005)	Yearly cost in millions	2000 Int$	DALYs averted per year (millions)	AFR-E	$C_M = C_S * million * \frac{pop_M}{pop_R}$	$D_M = D_S * million * \frac{pop_M}{pop_R}$
Uthman et al. (2011)	Cost	2008 US$	DALYs	Sub-Saharan Africa	$C_M = C_S * pop_{M_D}$	$D_M = D_S * pop_{M_D}$
Vassall et al. (2014)	Total cost	2011 US$	DALYs averted from 2004-2008 among a high-risk group of 154,425 individuals	India	$C_M = \frac{C_S}{154{,}425} * pop_{M_D}$	$D_M = \frac{D_S}{154{,}425} * pop_{M_D}$
Wilford et al. (2012)	Total cost for 2,780 patients	2007 US$	DALYs averted among 2,780 patients	Malawi	$C_M = C_S/2{,}780 * pop_{M_D}$	$D_M = D_S/2{,}780 * pop_{M_D}$

A3.4.3 Numbers of cases (or patients) and realistic coverage levels

Data on costs and DALYs averted by intervention enables the comparison of different interventions by cost-effectiveness. In order to determine the net benefit associated with each intervention, data on the size of the population that would benefit is also required. This data was obtained from CHAI from their 2014 costing. For each intervention the target population (e.g. pregnant women, women in need of PMTCT, etc.) in need is given for each of 192 interventions. CHAI also provided estimates of realistically attainable coverage levels obtained from a bottleneck analysis as part of their 2014 costing.

A3.4.4 Per case (or patient) costs

Although per patient costs could be obtained from the papers, as shown in Table A7, the costs provided by the papers may not reflect the cost of providing the intervention in Malawi. In addition, costs are often given as discounted lifetime costs. Malawi specific drug and supply costs for each intervention from the 2014 costing mid-term review were made available by Palladium and CHAI,

and these more accurately reflect the costs associated with each intervention for the purposes of deciding the budget. As such, the latter were used in estimating the scale of the package.

Using one source of cost data for ICER and net benefit calculations and another to determine the scale of the package can be cause for confusion. As an example the issue noted in Footnote 18 in Section 3 is presented here. If the costs used in ICER and net benefit calculations are the same as those used in calculating the cost of the package, forcing an intervention into the optimal package which is not already included on the basis of cost-effectiveness will necessarily reduce the total DALYs averted by the package. However, if separate costs are used (i.e. costs from a study are used to calculate ICERs and net benefit while Malawi specific annual costs are used to determine the cost of the package), the following scenario becomes possible: if the intervention that is being forced in has a lower per patient cost in Malawi than what was reported in the paper, and if it forces out interventions that have a higher per patient cost in Malawi than what was reported in the paper, this trade may actually increase aggregate DALYs averted.

In the report, disinvestment decisions are made on the basis of cost-effectiveness as calculated by using the cost data from the original source paper to determine an ICER. The least cost-effective interventions based on ICERs are removed until the package is within budget (where budget is based on the Malawi costs). This is reasonable as it is the lifetime costs and effects of different interventions that determine their relative cost-effectiveness, but it is the annual cost of provision that matters for each year's budget.

Ideally, Malawi-specific fully loaded, lifetime costs associated with delivering each intervention would be used in the calculation of ICERs. Obtaining this data is something to aspire for in future work. In the absence of reliable data on this, cost data from the region as presented in the original studies is a good second best option.

A3.5 Summary of data collected and future use by Ministry of Health and partners

The draft EHP presented in this report represents only a first take on the use of potentially available data. Ministry of Health and development partners must now take responsibility for updating, improving and ensuring appropriate use of the framework on an ongoing basis.

The interventions that have been included in the living data library were limited to those included in the 2014 EHP OneHealth Tool costing exercise conducted by CHAI. The rationale for this was that it ensured the availability of necessary data on number of cases (or patients), realistic coverage levels and per case (or patient) costs leaving only estimates of cost-effectiveness to be added, which could be obtained externally. In addition, this covered all interventions contained within Ministry of Health disease programme strategic plans. The OneHealth costing exercise included 167 interventions. From among these there were Malawi cost data for 133 (80%), coverage data for 143 (93%), and case or patient numbers for 143 (86%). This resulted in 117 interventions for which cost, coverage and case or patient numbers were available. ICERs were obtained for 67 (57%) of these 117 interventions. As cost-effectiveness data was not found for all of these interventions, and the plans do not represent an exhaustive list of all interventions that could be considered for implementation in Malawi, the data included so far in the library is, therefore, only a first take on the available literature and the search for additional data sources for a wider range of interventions must continue.

Moreover, the intervention lists and data sources used are time limited. They will have to be updated as new interventions become available, clinical and other evidence evolves, and prices change. National disease programme guidelines are intermittently revised as international recommendations change (e.g. World Health Organization clinical guidelines) and new evidence becomes available, and the funding environment and healthcare delivery will evolve through the lifetime of the Health Sector Strategic Plan. The Ministry of Health and partners will, therefore, need

to establish suitable processes for continually seeking the best evidence reflects the situation in Malawi to populate and update the library to support resource allocation decisions.

In the longer term, it should be hoped more evidence is generated within Malawi rather than having to rely on secondary sources drawn from healthcare systems that may differ in important ways for Malawi. As such the EHP framework can help to prioritise where new information in Malawi would be most valuable.

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