Accounting for health opportunity costs in key decisions in healthcare resource allocation in low- and middle-income countries

Jessica Marie Ochalek, BSc, MPH, MSc

PhD

University of York

Health Sciences

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Abstract

The concept of opportunity cost is fundamental to economic analysis. Opportunity costs exist because resources are scarce, and so their use in one way means they are not available for use in other ways. Economic evaluation methods that enable opportunity costs to be accounted for in decision-making in healthcare in high-income countries (HICs) are well-developed. However, methods are less well-developed to inform decisions in low- and middle-income countries (LMICs) despite the fact that it is in these countries where healthcare resources are most constrained and the potential health gains per additional resource spent on healthcare are greatest. This thesis provides methods to answer key policy questions for healthcare resource allocation in LMICs by extending existing frameworks and estimating key parameters required to inform them to enable health opportunity costs to be accounted for. It begins by providing empirical estimates of the marginal cost per unit of health produced by the healthcare system for LMICs, which were previously unavailable. How calculations of value founded on such estimates can be used to inform international guidelines about whether specific healthcare interventions should be provided in countries, whether and the extent to which these should be externally supported, and how to prioritise the development of new healthcare interventions for provision in LMICs is demonstrated. Next, the sources for empirical evidence to inform key parameter estimates for a framework of economic evaluation that accounts for the timing of costs and effects in a more appropriate way are identified, and the assumptions implicit in existing guidelines for economic evaluation are exposed and compared. Finally, a framework is developed to inform health benefits package (HBP) design that takes account of health opportunity costs and can analytically consider dimensions pertaining to equity, financing and implementation, while explicitly assessing key trade-offs in package design.

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Author's declaration

The five papers that form this thesis are listed below along with details of my contribution to each publication. I confirm that the integrative chapter exploring and linking the papers is entirely my own work. I declare that this thesis is a presentation of original work and I am the sole author. This work has not previously been presented for an award at this or any other University. All sources are acknowledged as references.

Study 1: Ochalek J, Lomas J, Claxton K.P., *Estimating health opportunity costs in low- and middle-income countries: a novel approach and evidence from cross-country data*, <u>BMJ Global Health</u>, 3(6), 2018.

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Chapter 1: Introduction and aims and objectives

A core objective of expenditure on healthcare is to improve population health.[1] All countries have the potential to improve population health through the provision of healthcare, but have limited healthcare resources with which to do this. Every decision therefore has an opportunity cost, which represents the best alternative use of the resources committed by the decision. Ensuring that decisions around how to allocate resources for health (whether between healthcare interventions or across the system more widely by investing in infrastructure or staff, for example) result in the greatest possible benefit to population health requires accounting for their health opportunity costs. Economic analysis offers practical, evidence-based methods to inform priority-setting in healthcare in a way that accounts for the opportunity cost of healthcare expenditure. Methods to do this in high-income country (HIC) contexts are well developed with a number of priority setting tools available to inform choices.[2,3] However, they are less well-developed to inform decisions in low- and middle-income countries (LMICs) despite the fact that it is in these countries where healthcare resources are most constrained and the potential health gains per additional resource spent on healthcare are greatest. The aim of this thesis therefore is to develop frameworks and parameterise them to enable health opportunity costs to be accounted for in key decisions around how to allocate resources for health in LMICs.

Economic evaluation methods have been developed primarily to inform the choice by national decisionmakers to fund or reject a new healthcare intervention in HICs,[3] and the importance of accounting for opportunity costs in funding decisions has begun to be recognized in policymaking, albeit also mainly in HICs. Many HICs have set up institutional bodies to undertake a formal process called health technology assessment (HTA) for assessing the value of a new healthcare intervention (also called a health technology).[4] Cost-effectiveness analysis (CEA), where the estimated costs and benefits of a healthcare intervention are judged against a decision-making threshold representing what is considered by the decision-making body to be good value for money, is an economic evaluation tool that typically forms a key component of HTA. For the decision-making threshold to inform decisions in a way that improves (rather than reduces) overall population health, it must reflect health opportunity costs.

Guidance from the National Institute for Health and Care Excellence (NICE) recommends a threshold reflecting the opportunity cost of healthcare interventions displaced by new, more costly ones, but applies a range of £20,000-30,000 per QALY based on previous decisions.[5,6] However, the UK Department of Health and Social Care uses an estimate of opportunity cost in the UK to guide fundings decisions in its Internal Impact Assessments.[7–9] In Norway, the National Council for Quality Improvement and Priority Setting in Health Care recommended that the Ministry of Health and Care Services adopt a cost per quality-adjusted life year (QALY) 'threshold' that reflected health opportunity cost in the Norwegian healthcare system following a public enquiry conducted in 2014 (the Norheim Commission), and the Norwegian Medicines Agency

(NoMA) subsequently adopted this into policy in 2015.[10] In Canada, proposed amendments to the Patented Medicines Regulations by the Patented Medicines Pricing Review Board included the use of a cost effectiveness threshold based on opportunity cost within the Canadian healthcare system.[11] In LMICs, the most commonly applied policy threshold is the range of 1-3x gross domestic product (GDP) per capita, which does not reflect health opportunity costs.[12] It was first proposed by the World Health Organization (WHO) for use with the WHO-CHOICE (CHOosing Interventions that are Cost-Effective) initiative, which pioneered the use of CEA for priority setting in health in LMICs.[13] While the WHO has more recently distanced itself from its prior guidance to use 1-3x GDP per capita as a threshold range, it has not replaced this guidance, leaving the decision to policymakers.[14,15]

A key parameter for calculating opportunity cost in healthcare is the marginal cost per unit of health produced by the healthcare system k_i, which enables the calculation of the expected net health impact of providing a healthcare intervention in a given country NHI_i. k_i is the relevant parameter whether the intervention is paid for via defunding some existing healthcare or through an expansion of the budget for healthcare, which could have been used for other healthcare. The NHI is the expected health gains from an intervention $\Delta health_i$ net of its expected health opportunity cost: the health that could have been gained with the additional healthcare system resources required to implement it ($\frac{\Delta C_i}{k_i}$). This is an essential calculation to determine whether the value added by a healthcare intervention is greater than the health that could have been gained by spending the money required to fund it elsewhere.

Equation 1.

$$NHI_i = \Delta health_i - \frac{\Delta C_i}{k_i}$$

Value can also be expressed in terms of the additional funding that would be required to achieve similar NHI: the net monetary value $N\$V_i$ is the amount of funding that would be required to deliver the same amount of net health gained.

Equation 2.

$$N\$V_i = k_i * \Delta health_i - \Delta C_i$$

These metrics of value capture the scale of the impact, combining information about the cost-effectiveness of the intervention and the size of the population that would benefit from it.

An empirical estimate of the marginal cost per unit of health produced by the healthcare system was first estimated by Claxton et al (2015) for the United Kingdom.[16] More recent work has followed a broadly similar approach using within country data to estimate this parameter for Spain, Australia, the Netherlands, Sweden, South Africa, China and Colombia.[17–23] The data requirements for this type of analysis are extensive and the time required to undertake the analysis is non-negligible - often measured in years rather than months.[24] To enable decision-making to be informed by such estimates now across a broader swathe of countries where such

data does not currently exist, alternative approaches for quantifying these values are required. This thesis therefore develops a novel approach to make the best use of available data from across countries to inform estimates of the marginal cost per unit of health produced by the healthcare system for a range of LMICs (Chapter 2).[25]

The availability of estimates of the marginal cost per unit of health produced by the healthcare system for a range of LMICs enables the value of healthcare interventions to be assessed across countries.[26] In HICs, decisions to fund an intervention are made at the country level, but with fewer resources to conduct HTA in LMICs, such decisions may be made on the basis of international guidance. The WHO sets international guidelines for healthcare that are intended to inform national decision making. An initiative of the World Bank that is now funded by the Bill and Melinda Gates Foundation (BMGF), the Disease Control Priorities Network (DCPN), also aims to assist countries in setting priorities. The DCPN book series Disease Control Priorities in Developing Countries (DCP1, 2 and 3) identifies interventions deemed high priority for funding across LMICs.[27] Finally, country-level decisions around which interventions to fund are also influenced by the United Nations (UN) Sustainable Development Goals for health.[28]

The application of the same guidelines and goals to all LMICs or sub-groups of LMICs does not properly account for the differences between countries in terms of the health opportunity costs they face due to differences in population burden of disease, age structure and life expectancies, funding available for health, development and infrastructure.[29] Value can be expressed as the scale of the potential NHI in a given country based on country-specific estimates of health opportunity costs. Aggregating country-specific value across countries where the NHI or N$V is positive (and the healthcare intervention would therefore be expected to be funded) gives the global NHI or N$V. Critically, understanding value internationally requires understanding value in each affected country.[26]

Understanding value in each affected country enables responses to key policy questions across LMICs to be informed in a way that ensures that they improve population health. For example, WHO guidelines aim to help countries achieve the best possible health outcomes, and are meant to take account of efficacy, effectiveness and potential harms of a healthcare intervention as well as acceptability, feasibility, cost and cost–effectiveness.[30] However, methods used by WHO to estimate cost-effectiveness do not properly account for health opportunity costs, and so following WHO guidelines to inform funding a healthcare intervention may generate a net health benefit in some of the countries that guidance is aimed at, but a net health loss in others. This can result in a healthcare intervention that is recommended internationally being deemed unaffordable in some countries. Some donors work to close the affordability gap by either subsidizing healthcare interventions (as in the case of Gavi, the Vaccine Alliance [hereafter Gavi]) or funding entire interventions or programmes of interventions (as in the case of the The Global Fund to Fight AIDS, Tuberculosis and Malaria [hereafter The Global Fund]). Gavi also acts on behalf of countries to negotiate prices of vaccines with manufacturers. Country-specific estimates of health opportunity costs can inform an assessment of the expected value of a

guideline across countries, the subsidies required for countries to follow it without reducing health outcomes, and the maximum price each country can afford to pay for a healthcare intervention. The latter is useful to inform priorities for developing new healthcare interventions, as is done by, for example, the BMGF.

The third chapter of this thesis illustrates this through an assessment of the expected NHI to countries of adopting the WHO's proposed 90-70-90 targets for cervical cancer elimination, which includes 90% coverage of human papillomavirus (HPV) vaccination among girls by 15 years of age using published estimates of the expected additional benefits and costs in each country and estimates of the marginal cost per unit of health produced by the healthcare system. This work demonstrates how calculations of value at the country-level and globally can therefore inform global guidelines (by e.g., the WHO), the provision of support for specific interventions (by e.g., GAVI and The Global Fund), and the development of new healthcare interventions for use in LMICs (by e.g., the BMGF).

Whether assessing the value of an intervention in one country or across countries, analysis to date has tended to apply a single, current estimate of health opportunity cost to the time stream of future costs and health benefits (converted to net present value using discounting) to calculate NHI. International guidelines that have been developed to guide economic evaluation in LMICs provide guidance around the discount rate to use to obtain the present value of health benefits and costs, but do not explicitly recommend accounting for growth in the marginal cost per unit of health produced by the healthcare system. Using a single estimate of health opportunity cost based on the current value of the marginal cost per unit of health produced by the healthcare system embeds implicit assumptions about economic growth that are likely implausible, especially in LMICs with high growth economies. This has implications both in terms of how opportunity costs can be expected to evolve over time and how account can be taken of the timing of the costs and health benefits of a healthcare intervention.[31]

Chapter 4 of this thesis identifies the sources for empirical evidence to inform key parameter estimates across countries and over time that are required to be able to apply a framework for economic evaluation (not part of this thesis) that clarifies the distinct roles of different parameters required for economic evaluation, including the marginal cost per unit of health produced by the healthcare system and the consumption value of health, in evaluating a healthcare intervention.[31] The framework was developed with the support of the BMGF to inform the reference case guidelines for benefit-cost analysis in global health and development. This chapter also demonstrates how using existing guidelines may result in different decisions, exposing the assumptions implicit in applying existing guidance around the discount rate to use to obtain the present value of health benefits and costs.

The same principles that inform the assessment of the value and pricing of a particular healthcare intervention also apply at the healthcare system level. A key policy objective of healthcare expenditure in LMICs is Universal Health Coverage (UHC), and consideration of funding a healthcare intervention forms only one piece of this larger puzzle. Achieving UHC is

one of the UN Sustainable Development Goals, and entails providing essential, quality healthcare to the whole population ensuring that no one incurs financial hardship in obtaining it.[32] The trade-offs on the path toward achieving UHC are often visualized using the "WHO Cube", the three dimensions of which are: what treatments to provide (the depth of coverage); to what proportion of the population (the breadth of coverage); at what price to patients (the height of coverage).[33]

A key policy tool for achieving UHC are health benefits packages (HBPs), which address one dimension of the cube, the depth of coverage, by defining the range of treatments to which the population is entitled.[34] Setting HBPs in LMICs has been supported by organizations such as DCPN, Center for Global Development, and the Inter-American Development Bank.[27,34,35] In practice, the HBPs set in countries have tended to overpromise compared to what is feasible to fund with the available budget and given other constraints (such as levels of infrastructure and human resources).[36] This was the case in Malawi for both its previous two HBPs.[37,38]

This thesis produces a framework to inform key questions in setting a HBP.[39–41] Through a five-week visit at the Ministry of Health (MoH) in Malawi, key questions in HBP design in Malawi were determined and a framework developed in collaboration with individuals in the MoH, which, using an estimate of the marginal cost per unit of health produced by the Malawian healthcare system and data from Malawi, can analytically consider dimensions pertaining to equity, financing and implementation (Chapter 5). The creation of a HBP is critical to the effective implementation of UHC; however, UHC policy also requires consideration of the other dimensions of the cube. This thesis therefore also sets out an approach to informing policy on the breadth of the population to be covered by UHC, as well as the depth (i.e., range of interventions). The framework set out in Chapter 5 is extended to reflect increases in the cost of providing healthcare interventions to poorer, more difficult to reach populations. This allows an assessment of the trade-off between extending coverage of interventions to these groups (extending breadth) compared to providing additional interventions (extending depth) (Chapter 6).[42]

Aims and objectives

The aim of this thesis is to develop frameworks and parameterise them so that health opportunity costs can be accounted for in key decisions around how to allocate resources for health in LMICs. This is achieved through the following objectives, which are directly informed by key policy questions in LMICs:

- Estimate the marginal cost per unit of health produced by the healthcare system for a range of LMICs (Chapter 2).
- Demonstrate how calculations of value at the country-level and globally can therefore inform global guidelines (by e.g., the WHO), the provision of support for specific interventions (by e.g., GAVI and The Global Fund), and the development of new healthcare interventions for use in LMICs (by e.g., the BMGF) (Chapter 3).

- Identify the sources of empirical evidence to inform key parameter estimates across countries and over time that are required to be able to apply a framework for the economic evaluation of healthcare interventions that accounts for growth in the marginal cost per unit of health produced by the healthcare system, and reveals assumptions around growth in this parameter implicit in existing guidelines for economic evaluations (Chapter 4).
- Develop a framework to inform health benefits package (HBP) design that takes account of health opportunity costs and can analytically consider dimensions pertaining to equity, financing and implementation (Chapter 5).
- Extend the framework set out in Chapter 5 to offer an explicit assessment of the trade-off between extending coverage of interventions to these groups compared to providing additional interventions (Chapter 6).

Each of chapters 2 through 6 gives the context from which the research question is drawn ("Background"), the methods used to address it ("Methods"), the findings ("Results"), the impact these have had ("Impact"), and any remaining or resulting questions ("Directions for future research"). The last chapter of this thesis discusses the findings of each chapter within the larger context of decision-making in health in LMICs and provides suggestions for future streams of research that arise from this work.

Chapter 2: Health opportunity costs in low- and middle-income countries

Background

An understanding of the health effects of an increase or decrease in health care expenditure can be used to inform a wide range of policy questions around how to allocate resources for health in LMICs. A key question is whether a healthcare intervention should or should not be funded through collectively pooled funds for healthcare. This is often operationalized by comparing the ratio of expected costs to health benefits against a policy threshold. In LMICs, the most commonly applied policy threshold to inform this decision is the range of 1-3x GDP per capita initially proposed by the WHO for use with the WHO-CHOICE initiative.[13] This range is heuristic and does not reflect the opportunity cost of spending.

The opportunity cost of providing or funding a health technology is the health benefits that could have been gained had the money required to fund it been spent elsewhere in the healthcare system.[43] In practice, exactly which other healthcare intervention(s) might be given up to free up money to fund the new healthcare intervention is not typically known. This can instead be informed by an empirical estimate of the marginal cost per unit of health produced by the healthcare system k_i. This is the amount of health that would be gained by an increase in expenditure (or forgone by a decrease), and is the appropriate parameter regardless of whether the money required to fund a new healthcare intervention comes from within a fixed budget or represents an increase in the budget.

Empirically estimating k_i is precisely what has been done in studies considering individual countries to date: the UK for the National Health Service (NHS), where this was first estimated; and then in Spain; Australia; The Netherlands; Sweden; South Africa; Colombia; China and Indonesia (not part of this thesis).[16,17,20–23,44–46] Obtaining a causal effect of a change in health expenditure on health outcomes has a number of methodological challenges. An increase in health expenditure would be expected to lead to an improvement in health outcomes; however, it is also possible that poorer health outcomes lead to increases in health expenditure (i.e., simultaneity bias). A second major challenge is controlling for all possible external factors that might affect health. The different empirical approaches to estimating this and the associated assumptions taken by existing published studies for individual countries are reviewed and summarised in Edney et al. (2021) (not part of this thesis).[47]

The data requirements mean that it is not possible to undertake this type of analysis for many LMICs. However, a wealth of literature has assessed the effect of health expenditure on health outcomes using international data,[48] although findings have been inconsistent (owing largely to the methodological challenges associated with estimation). More recent studies (both international and five of the eight country studies reviewed by Edney et al. (2021)), have employed an instrumental variable (IV) approach.

Methods

We identified a paper by Bokhari et al (2007), which applies the IV method to international data. It develops methods used in the earlier literature, such as Filmer and Pritchett (2000), in important ways. For example, by allowing for non-constant elasticity effects by country or income group and allowing for country's income to be endogenous. The analysis conducted by Bokhari et al (2007) could be extended to include as estimands measures of mortality that could plausibly be translated into a generic measure of health, which is what is needed to inform the health opportunity cost of decisions that may concern a wide range of disease areas, populations and interventions (some of which will have effects on health beyond mortality and others that may only affect morbidity, for example).

Generic measures of health incorporate effects on both survival and morbidity. The most widely used measures are Quality Adjusted Life Years (QALYs) and Disability Adjusted Life Years (DALYs). The former quantifies health to be gained while the latter quantifies burden of ill health to be averted, and they are roughly interchangeable.[49] International data are available to support the analysis of DALYs at the international level from the Global Burden of Disease (GBD) project, and we therefore use this measure.

Calculating k_i requires a series of steps, each requiring their own set of assumptions. The methods have their foundations in the seminal work by Claxton et al (2015), which estimates k_i for the UK healthcare system.[9] The steps are detailed in the peer-reviewed journal publication and Centre for Health Economics (CHE) Research Paper that preceded it, and summarised briefly below.[50,51]

First, an estimate of the effect of expenditure on health is required. Our analysis starts by extending the dataset generously shared by Farasat Bokhari and his co-authors to be able to estimate the effect of expenditure on not only under-5 and maternal mortality (in their original analysis), but also adult male and adult female mortality, as well as the survival burden of disease (i.e., years of life lost, YLL), the morbidity burden of disease (i.e., years of life disabled, YLD) and overall burden of disease (i.e., DALYs) for the same year (2000). We then apply the estimated effects to determine the DALYs averted using data for each individual country from GBD using four different approaches, which enable a comparison of directly estimating DALY effects and of using mortality effects as a surrogate for them.[52]

Results

The results of this work provide estimates of k_i presented in terms of cost per DALY averted for 97 LMICs. The key finding is that thresholds that reflect health opportunity cost (i.e., are based on estimates of k_i in each country) are likely substantially lower than the 1-3x GDP per capita heuristic threshold that has been widely used by global bodies making recommendations, purchasing healthcare interventions or prioritising the development of new ones as well as decision makers in LMICs.

The four approaches to calculating DALYs averted from the estimated effects on mortality, YLL, YLD and DALYs employ slightly different assumptions. Comparing the approach that uses the effect of expenditure on mortality against the approach that uses the effect of expenditure on DALYs helps to inform whether it is reasonable to use estimates of the effect of expenditure on mortality as a surrogate for likely survival (YLL) and morbidity (YLD) effects. This is relevant to most studies that investigate the relationship between mortality and health expenditure using high-quality within-country data, as while this overcomes some of the difficulties and challenges of estimation based on aggregate country-level data, mortality is typically the only health outcome measure available.[47]

We find that the DALYs averted calculated using the approaches based on the estimated effect of expenditure on mortality and on DALYs are more similar to each other than the DALYs averted calculated using the approaches based on the estimated effect of expenditure on survival (YLLs) and morbidity (YLD). We interpret this as suggesting that using estimates of the mortality effect of changes in health expenditure as a surrogate for both likely survival (YLL) and morbidity (YLD) effects may not be unreasonable although with additional uncertainty.

Impact

The early dissemination of these results influenced the WHO decision to formally step back from recommending the use of 1-3x GDP thresholds for decision-making in LMICs.[14,53] They have directly affected how the World Bank makes recommendations about the cost-effectiveness of health care interventions, with the most recent edition of *Disease Control Priorities*, *DCP3*, categorising interventions according to cost-effectiveness and use as their most "stringent" category a maximum threshold value of $250/DALY averted intending to reflect health opportunity costs based on this work.[54] It has also informed prioritisation at the BMGF, and has directly informed the development of the health benefits packages of the Ministries of Health in Malawi and Ghana.[55,56] The research has also inspired similar work in other countries (South Africa, China, Colombia and Indonesia), which cite this research as informing the methods used to calculate the health effects of changes of expenditure and the interpretation of the results.[19,23,45,46]

Directions for future research

How these estimates may be applied to assess the value of a healthcare intervention in each country is well-developed as discussed in the Introduction. However, how they should be used to inform recommendations or decisions made on behalf of groups of countries, such as the WHO recommendations or BMGF decisions about prioritising the development of healthcare technologies is less developed. This gap is addressed by Chapter 3 of this thesis.

Chapter 3: Assessing the value of human papillomavirus vaccination in Gavi-eligible low- and middle-income countries

Background

Blanket recommendations made by international organisations, such as the WHO, around the adoption of healthcare interventions across countries traditionally do not account for the likely health opportunity costs in those countries. As a result, they risk recommending health technologies that are not cost effective in some countries, even given existing donor mechanisms intended to support their affordability. There is a need for an assessment of the impact of blanket recommendations on net health effects for individual countries to which they apply and the maximum price that each country can afford to pay for a health technology to be cost-effective. The latter can further inform donor mechanisms that exist to close the affordability gap for countries to provide interventions that are recommended but are not necessarily affordable or cost-effective in their setting.

To expose the risk of blanket recommendations that do not account for opportunity costs, we apply a real-world example by assessing the expected net health impact (NHI) to countries of adopting the WHO's proposed 90-70-90 targets for cervical cancer elimination. The targets include 90% coverage of human papillomavirus (HPV) vaccination among girls by 15 years of age using published estimates of the expected additional benefits and costs in each country and estimates of the marginal cost per unit of health produced by the healthcare system k_i. We illustrate how assessments of value can be used to inform global guidance or recommendations and pricing negotiations by assessing four real-world policy options.

Methods

We set out how value can be assessed in terms of health (see Introduction Equation 1) and the equivalent financial value of that health to the healthcare system (see Introduction Equation 2) first within each country and then across countries.

We calculate the NHI of providing HPV vaccination to the eligible population in each country using estimates of the additional health benefits of HPV vaccination, the additional cost, and estimates of k_i from Chapter 2 of this thesis. NHI is measured in terms of DALYs averted.

We use these estimates to calculate the aggregate net effects of providing the HPV vaccine in a group of countries (e.g., all countries in a given income category or all Gavi-eligible countries) by summing the estimated NHI (Equation 3) or net dollar value by country (Equation 4).

Equation 3.

$$\sum_{i=1}^{n} NHI_i = \sum_{i=1}^{n} \left(\Delta DALYs_i - \frac{\Delta C_i}{k_i} \right)$$

Equation 4.

$$\sum_{i=1}^{n} N\$V_i = \sum_{i=1}^{n} k_i * \Delta DALYs_i - \Delta C_i$$

This enables the quantification of the value of achieving the WHO recommendation of 90% coverage of HPV vaccination in Gavi-eligible countries given the price of the vaccine, which we assess value at the average market per dose procurement prices (US$25 per dose) and using current Gavi-negotiated per dose procurement prices (US$4.50 per dose).

We also determine the maximum price each country could afford to pay for HPV vaccination to, at minimum, generate no net health harm. This is the price at which the N$V to the healthcare system is zero. Finally, we consider tiered pricing (e.g., setting prices for groups of countries). The resulting value in each country can be aggregated across countries to inform the global value of providing HPV vaccine at a given price to all countries or using tiered or country-specific pricing policies.

Results

We find that achieving the WHO recommendation of 90% coverage of HPV vaccination in Gavi-eligible countries at the average market per dose procurement prices (US$25 per dose) would result in net health losses in most countries, with an aggregate net burden of 38 million DALYs resulting across countries.

The price reduction required for all Gavi-eligible countries to be able to afford to provide HPV vaccination (i.e., so that doing so generates, at minimum, no net health loss for the healthcare system ranges from US$2 to US$26 (2019 US). If the manufacturer and/or a global donor were to fund the difference for each country, it would cost US$9.3 billion (2019 US). The same money could avert 49 million DALYs if spent on existing interventions in these countries instead.

If prices were negotiated by country income-groups, the lowest price required for HPV vaccination to be cost effective in any of these countries in the income-group would need to be applied to all countries in the group. If the manufacturer and/or a global donor were to fund the difference for each country, it would cost US$14.7 billion (2019 US). More net health benefits would be generated across countries than from utilizing country-specific prices; however, the same money could avert 70 million DALYs if spent on existing interventions in these countries instead.

From a public health perspective, country-specific pricing represents a better option because the cost difference between country-specific pricing and country-group pricing, $5.4 billion (2019 US), could generate health gains in addition to those generated through the provision of HPV vaccination.

The NHI and net monetary impact (N$V) of achieving the WHO recommendation of 90% coverage of HPV vaccination in all Gavi-eligible countries at current Gavi-negotiated prices (US$4.50 per dose, 2019 US), results in positive NHI in most countries. Gavi's negotiations on behalf of countries eligible for its support have succeeded in making adhering to the WHO guidance around HPV vaccination a beneficial aim for most countries.

This analysis can inform donor decisions around the extent to which to support countries' provision of recommended existing health technologies by, for example, Gavi, and potentially the development of new technologies by, for example, BMGF and other donors. This work demonstrates the need to understand value in each affected country in order to understand value internationally.

Impact

This chapter responds to a policy need from the BMGF for methods to better inform funding priorities for the development of competing potential healthcare interventions in the development pipeline. The organisation funds the development of promising healthcare interventions with the potential for application across a range of LMICs. Their existing strategy informed prioritization decisions by providing information for each intervention on the cost per DALY averted, likelihood of success, and scale of the burden of disease that would be expected to be averted.[57] What was missing was an assessment of where costs fall and their associated opportunity cost. The target product profile data that informs BMGF development decisions is proprietary, but the framework developed to inform product development priorities is relevant more widely for recommendations made by international organisations (e.g., WHO) and the donor organisations that work to help countries achieve these recommendations. This analysis informed the BMGF executive board prioritization of product development decisions following the presentation of this work to members of executive board in April 2019].[58]

Directions for future research

This paper uses estimates of health opportunity cost based on k_i for a single year, implicitly assuming that there is no real growth in k_i. This is unlikely to be the case; however, at the time of this research, there were no estimates of how k_i is likely to evolve and no guidance to indicate how growth rates might differ across countries. Thus, there is a need for empirical evidence to inform estimates across countries and over time. This need is addressed by Chapter 4 of this thesis.

Chapter 4: Accounting for country- and time-specific values in the economic evaluation of health-related projects relevant to low- and middle-income countries

Background

Most healthcare interventions incur costs and/or health outcomes in future years as well as in the current year (e.g. a vaccine may incur costs in the initial year and health benefits only years later). Identifying a need for better guidance around the appropriate analysis of time streams of the effects of interventions, the BMGF supported the development of a framework, set out in Claxton et al (2019) [31] (not part of this thesis) to inform the Reference Case Guidelines for Benefit-cost Analysis in Global Health and Development. The framework clarifies the roles of distinct evaluation parameters for analyzing healthcare interventions and interventions with costs and effects beyond health and identifies relevant evidence and gaps in the evidence to inform each parameter. One important gap that was found to exist was in how estimates of the marginal cost per unit of health produced by the healthcare system k_i (estimated in Chapter 2) might evolve over time.

This chapter contributes to the evidence base for conducting economic evaluations of healthcare interventions by providing estimates of k_i over time for a range of LMICs ($k_{i,t}$). This evidence is then applied to the analysis of a hypothetical healthcare intervention using the framework set out in Claxton et al (2019) [31] (not part this thesis) to demonstrate how the application of existing guidance for economic evaluation may tend to underestimate the value of health-related projects in LMICs.

Methods

Projections of $k_{i,t}$

Prior to this research, estimates of $k_{i,t}$ for future years had not been available. While changes in this parameter, $k_{i,t}$, (and its implications for the discount rate for health, $r_{h_{i,t}}$) are determined by a number of factors,[59] it is reasonable to expect that there will be some indirect relationship with a measure of economic output such as GDP per capita since there are more resources in society that can potentially be devoted to health care. This chapter offers a practical method for obtaining future projections of $k_{i,t}$ for 95 LMICs from 2015 to 2040 by analysing the relationship between estimates from Chapter 2 for 2015 and GDP per capita as well as total fertility rate, for both of which projected values exist from Dieleman *et al* (2017), across countries, and sub-groups of countries.[60]

Applying the framework

We apply these estimates to an illustrative example and compare the results to approaches based on existing guidelines for conducting economic evaluations in LMICs, both where the objective is to improve health and where it is to improve consumption: the International Decision Support Initiative (iDSI) Reference Case for Economic Evaluation, WHO immunization

guidelines, WHO GCEA guide, and the Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development in LMICs.[61–64]

Results

Our projections show that the expected rate of growth in $k_{i,t}$ differs across countries and over time, with non-linear positive growth expected in most countries but negative non-linear growth expected in some years in some countries.

Our assessment of the assumptions implicit in existing guidelines finds that although the iDSI Reference Case for Economic Evaluation recommend accounting for opportunity costs in evaluations, it gives no consideration of how the marginal cost per unit of health produced by the healthcare system is likely to evolve over time in each country resulting in an implicit assumption of zero growth.[63] The WHO GCEA guide implies an assumption of the consumption value of health remaining constant in real terms.[61] The WHO immunization guidelines do not explicitly recommend accounting for opportunity costs in evaluations at all. They also propose differential discounting for health gains (at 0%) and discount rates of 3% for healthcare costs and consumption.[62] The use of differential discounting in this way implies an assumption of 3% annual growth in both the marginal cost per unit of health produced by the healthcare system and the consumption value of health. The Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development in LMICs recommends that health is valued using the consumption value for health with guidance on how this may change over time, but that the discount rate applied to consumption is a constant 3% for all countries.[64,65]

Application to a simple hypothetical health-related project allowed a comparison of the results of evaluation based on existing guidelines for conducting economic evaluations in LMICs with those based on country and time specific estimates of key parameters. We find that applying existing guidelines is likely to underestimate the value of health-related projects on account of not allowing for expected growth in the marginal cost per unit of health produced by the healthcare sector. Whether an intervention was found to be cost-effective could also vary depending on which guideline was used.

Impact

This work was part of the answer to a call from the BMGF to inform the reference case guidelines for benefit-cost analysis in global health and development. This chapter is the first published work to provide estimates of the marginal cost per unit of health produced by the healthcare system for future years $k_{i,t}$, and demonstrates the consequences of applying existing guidance around accounting for the timing of costs and effects in terms of the potential harms to population health.

Directions for future research

There are a number of directions for future research that spring from this work. The projections of $k_{i,t}$ use pre-pandemic projections of GDP and should be updated when new projections of GDP are available.

We also use a hypothetical example to demonstrate how the application of different guidelines for evaluation might affect an assessment of cost-effectiveness. An application to data from a real healthcare intervention with costs and benefits far into the future would provide another interesting demonstration that might seem more tangible to the end users of economic evaluations as well as the groups that produce guidelines to guide their production.

Chapter 5: Supporting the development of a health benefits package in Malawi

Background

Methods for informing the decision to fund a given healthcare intervention from among a set of mutually exclusive alternatives are well established and estimates of $k_{i,t}$ to inform these decisions are now available for a wide range of countries for a range of years up to 2040 from Chapters 2 and 4. However, decisions around how to allocate scarce resources for healthcare to a wider set of healthcare interventions using these estimates, for example, within a Health Benefits Package (HBP), lack a widely accepted method. HBPs are a commonly used policy tool in LMICs to define which healthcare interventions are made available to the population using publicly pooled funds for healthcare. However, they often overpromise what can feasibly be provided given resource constraints. There is, therefore, a need for an analytical framework to guide the design of HBPs that can identify the potential value of including and implementing different healthcare interventions and the trade-offs implicit in different potential packages.

Malawi introduced its first HBP (called the Essential Health Package, EHP) in 2004. It was followed up with a second EHP in 2016. Both were, however, unsustainable, estimated to cost between 83% and 182% of total health expenditure, of which the EHP forms only a part.[38] This resulted in implicit rationing with inequitable variations in access to care and high value interventions not being available.[55] For the 2017-2022 Health Sector Strategic Plan (HSSP), the Ministry of Health looked to develop a HBP that improved population health to the greatest degree possible given the resources available.

In collaboration with the Ministry of Health, this thesis develops an analytical framework grounded in the principles of economic evaluation that answers key questions in HBP design. As part of this collaboration, I travelled to Malawi on several occasions to meet with and present to policymakers including a five-week period during which I was based in the Ministry of Health. Along with numerous informal meetings, I presented a 'Framework for the Development of an EHP for Malawi' at the HSSP II Core Team meeting at the Ministry of Health in Lilongwe, Malawi in March 2016. I also presented 'A Revision of the EHP for 2016 Onwards' and 'Supporting the Development of an EHP for Malawi' at workshops in Lilongwe, Malawi in June and November 2016 respectively. A news article about the first workshop is posted on the CHE webpages at https://www.york.ac.uk/che/news/2016/che-malawi-workshop/.

Through this close collaboration, it was determined that key questions for the Ministry of Health included: what is the appropriate scale of the HBP; which interventions represent 'best buys' and should be prioritized; where should investments in scaling up interventions and health system strengthening be made; should the package be expanded; what are the costs of the conditionalities of donor funding; and how can objectives beyond improving population health be considered. The framework developed to inform answers to these is applied to data from Malawi.

Methods

The framework uses metrics of value founded on an understanding of the health opportunity costs of the choices faced to quantify the scale of the potential net health impact (NHI) measured in terms of net DALYs averted or the amount of additional healthcare resources that would be required to deliver similar NHI with existing interventions (N$V) introduced in chapter 1 (equations 1 and 2). These metrics of value account for the scale of the net health (or net financial) impact, incorporating data on costs, effects and the size of the population that stands to benefit from the healthcare intervention, which accounts for burden of disease. We apply an estimate of k for Malawi from Chapter 2, which represented the most recently available estimate at the time of this work.

We rank interventions according to their expected NHI, which enables priority interventions to be identified, and demonstrate how results differ compared to ranking by ICER.

Second, we apply data on the extent to which cost-effective healthcare interventions would likely be implemented in reality to calculate the value of implementation efforts and health system strengthening. In Malawi, as in many other countries, constraints (e.g., infrastructure, human resources, geography, etc.) mean that some healthcare interventions are not accessible to the full population in need of them. This also informs the maximum that should be spent on scale up s of an intervention i for it to remain a cost-effective use of resources. This is simply the $N\$V$ of the intervention if fully implemented f minus its $N\$V$ at its realistic implementation level p as in Equation 9.

Equation 9.

$$N\$V_i^s = N\$V_i^f - N\$V_i^p$$

Aggregating across interventions as in Equation 10 gives the value of health system strengthening.

Equation 10.

$$\sum_{i=1}^{n} N\$V_i = \sum_{i=1}^{n} N\$V_i^s$$

Third, we show how estimates of k can be used to inform the value of expanding the budget for healthcare (or how much health would be expected to be given up if from contracting the budget) in Malawi.

Fourth, using potential policy options as examples, we show how quantifying the NHI of potential donor funding arrangements can inform discussions with donors with an aim to better align donor funding with government health spending objectives.

Finally, we describe how value can be weighed against gains in other non-health objectives that result from the inclusion of an intervention.

Results

Our results show that ranking interventions according to net DALYs averted results in a different ranking than ranking according to ICER (i.e., using a league table approach). League table approaches to determining HBPs have been put forth previously to inform HBP design,[61,66] and risk mis-prioritising interventions given they rank according to ICER, which is especially relevant in contexts where HBPs overpromise and some interventions included in the package are not provided in part or in full. Similarly, prioritising interventions based on burden of disease risks missing off interventions that generate high health gains. Using the metrics of value proposed here, which account for health opportunity costs, overcomes these issues. Based on our findings, we expect that investments in health system strengthening would generate high value. Finally, our results show that donor funding arrangements that are aligned with an objective of health maximisation will generate more health gains than arrangements specifically for interventions whose health opportunity costs are greater than the health gains they are expected to generate.

Impact

The framework developed as part of this thesis was handed off to a Ministry of Health Technical Working Group tasked with developing the 2017-2022 HSSP for use in informing the 2017-2022 Essential Health Package, a core part of the HSSP.[55]

I received an official Vote of Thanks from the Secretary for Health for this work stating: "We acknowledge the visits you made to gain a first-hand understanding of the context as well as the remote support you provided. Colleagues in the Department of Planning and Policy Development rate the EHP report as one of the best technical documents that have been produced for the Ministry." (See Appendix 1). I subsequently supported an Overseas Development Institute (ODI) Fellow's evaluation of Ghana's HBP.[67]

The work has also received interest from other policymakers, and I've presented it to audiences from the East, Central and Southern Africa Health Community, the Inter-American Development Bank, the Indonesian Health Economics Association, and the ODI. It has since been cited in informing an assessment of Ghana's HBP and the introduction of HTA in Tanzania.[68]

Directions for future research

In Malawi, around half of the interventions included in previous HBPs were found to be only provided to or accessed by a portion of the population in need. While the framework offers a means to assess the value of scaling up the provision of interventions to the full population in need, it does not formally incorporate potential non-linearities in the costs and benefits of interventions at different levels of provision or differential weights for the health benefits generated for different socioeconomic groups where levels of coverage differ for different

socioeconomic groups. Formally incorporating these represents a valuable extension of this work and is address by chapter 6.

The evidence base for the HBP is taken as given in this work, but is, in reality, uncertain. Funds available for research to address this uncertainty are limited. Recent analysis (not included as part of this thesis) extended this work to inform how research priorities can be incorporated within HBP design.[69]

As shown in the case of Malawi, where the framework was adopted to inform the country's HBP which forms a core part of the HSSP, in practice, it is difficult to limit the package to the extent that is possible to cover the population in need for each intervention in full. Instead, a wider set of interventions is included, but not all of the population in need for each intervention access them. Therefore, trade-offs between expanding the number of interventions covered and the extent to which the population in need of each intervention is covered must be made. This requires the development of further methods to quantify this trade-off.

Finally, the development of a dynamic, whole healthcare system model could account for interdependence between healthcare interventions and the effects of health system strengthening interventions.

Chapter 6: Squaring the cube: Towards an operational model of optimal universal health coverage

Background

HBPs usually promise a set of interventions available to the entire population (i.e., at "full coverage") paid for through collectively pooled funds for healthcare. The promise of full coverage is aligned with the definition of Universal Health Coverage (UHC); however, in practice interventions are often only available to part of the population. This implicit rationing of interventions may occur where the least well off are less able to secure access to care than the most well off.

Implementing UHC poses tough policy choices about: what treatments to provide (the depth of coverage); to what proportion of the population (the breadth of coverage); at what price to patients (the height of coverage). The framework set forth in chapter 5 offers a means to assess the value of scaling up the provision of interventions to the full population in need, but assumes costs and benefits are linear. In reality, it may cost more to provide an intervention to the least well off who may live in remote areas with less infrastructure (e.g., clinics, roads, electricity and hospitals).

Guided by the principles of economic evaluation, this chapter extends the framework developed in Chapter 5 by allowing for variations in both the costs and the benefits of healthcare interventions according to the deprivation level of the population. We illustrate the use of a theoretical mathematical programming model to analytically derive the optimal balance between the range of healthcare interventions provided (the depth of coverage) and the proportion of the population covered by each (the breadth of coverage) for a hypothetical East African country. Consistent with reflecting policy objectives, the optimal balance is defined as that which achieves the greatest health.[1,55]

Methods

Using data from WHO on the costs and benefits of treatments at different coverage levels in the AFR-E region, we model a hypothetical health care system with a population of 25 million and an assumed exogenously fixed discretionary budget of $15 million (2015 US) that may be spent on any combination of the 16 interventions listed over a range of coverage levels. We assume that interventions are independent and coverage levels are mutually exclusive.

We present three scenarios for comparison. The first allows coverage levels to vary. In the second scenario, we allow coverage levels to vary and apply differential equity weights to benefits. We assume for the purposes of illustration that patients who are the most difficult to reach are also the poorest, and apply a weight of four to the benefits in the last decile of coverage and a weight of two to patients in the penultimate decile. The third scenario reflects common practice in HBP design: interventions are either provided at 95% coverage or not at all. We present the optimal package (i.e., what treatments are covered at what level of coverage) for

each scenario. This enables the quantification of the health gains (measured in terms of DALYs averted), offering transparency to decisions around HBP design.

Results

Figure 1 shows the results of the optimization, and given the budget, what coverage level a health maximising decision maker would cover each intervention at.

Figure 1. Coverage levels for each intervention
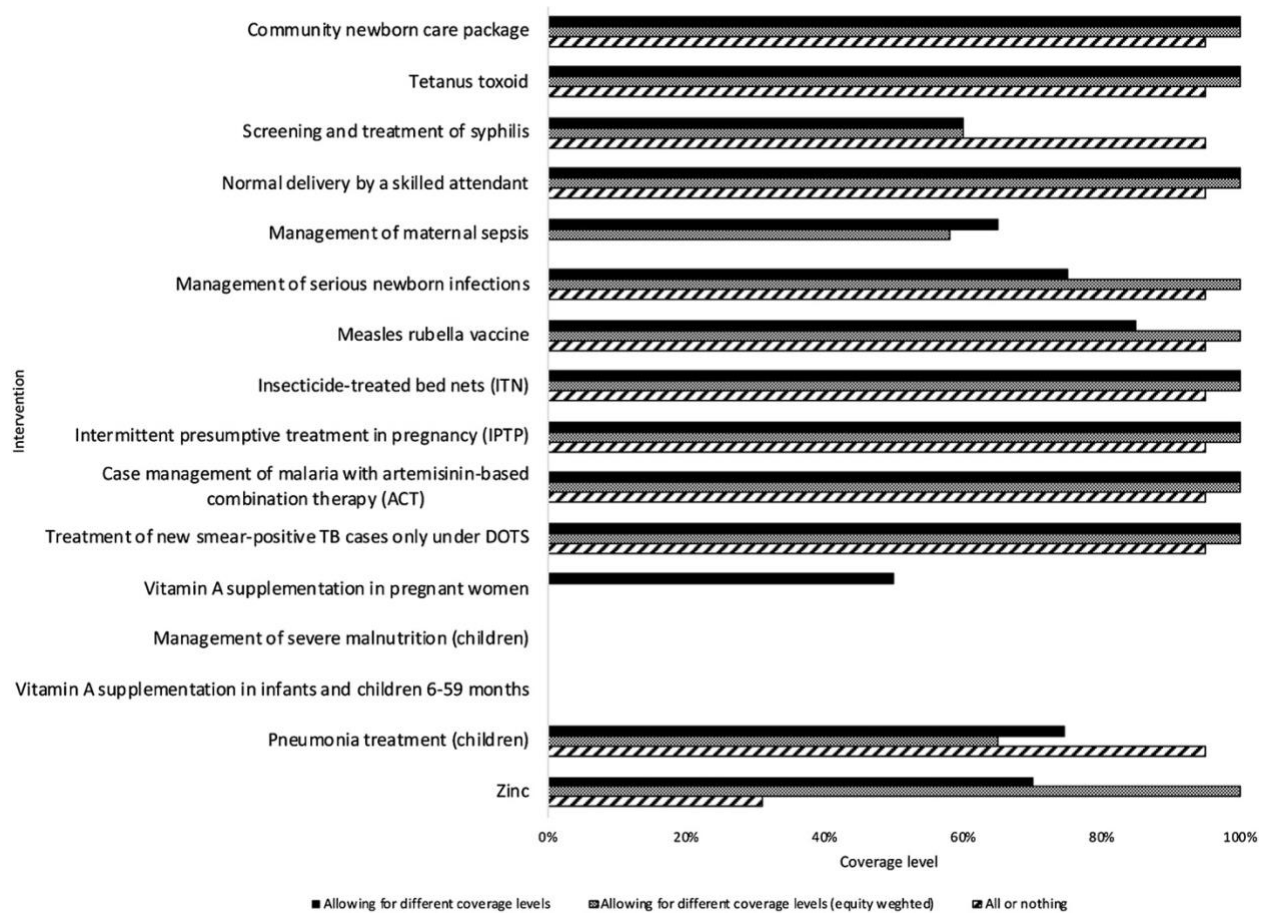
The first scenario maximises health given how costs and benefits would vary by coverage level and is shown by the black bars. In this scenario, seven of the 16 possible interventions are provided at 100% coverage while another seven are provided at lower levels of coverage and two are not provided. This scenario generates the greatest health, averting more DALYs than scenarios two and three.

In the second scenario (the grey bars) differential weights are applied to reflect equity concerns. In this scenario fewer interventions are provided, but those that are covered tend to be cover a

greater proportion of the population, ensuring more coverage of the more difficult to reach portion of the population. This scenario results in fewer DALYs averted than the first scenario, but this may be justified by population preferences for improvements in equity.

The third scenario reflects common practice. It results in the lowest total DALYs averted across the population and also has implications for equity, failing to cover the most difficult to reach 5% of the population for any intervention.

Impact

This paper contributes to the wider body of literature looking to inform resource allocation decisions in healthcare in countries working toward UHC. It shows the need for decision-makers to consider the implications of implicit rationing of the interventions provided through a HBP, and provides a method with which to do that.

Directions for future research

This paper addresses two dimensions of UHC: what interventions to provide (the depth of coverage); to what proportion of the population (the breadth of coverage). Further work could address the third dimension, at what price to patients (the height of coverage) interventions should be provided. This would require additional data on the price elasticity of demand for different healthcare interventions, which, if available, would square the cube on financial protection.

Chapter 7: Discussion and Conclusion

This section describes how the papers presented in this thesis together form a coherent body of work, summarizes their contributions to the to the academic health economics literature and their policy impact. It concludes with a discussion of potential future research in this area arising from the limitations of these papers.

This thesis makes an original contribution to knowledge and forms a coherent body of work by developing and parameterising frameworks to enable health opportunity costs to be accounted for in key decisions about how to allocate resources for health in LMICs. The concept of opportunity cost is fundamental to economic analysis. Application of this in informing healthcare policy requires careful consideration and empirical estimates of the marginal cost per unit of health produced by the healthcare system. This thesis makes the most of the data that are available to empirically estimate this parameter and other key parameters for a range of countries and over time. Using these estimates, it goes on to explore the implications for healthcare policy. In particular, the work from this thesis informs decisions about how to allocate scarce resources for health to particular interventions within a country and across countries. It shows how estimates of the NHI of particular interventions are valuable for informing recommendations made across countries, as well as pricing and subsidies. Finally, it demonstrates how the same principles also apply at the healthcare system level, and can be used to inform HBP design accounting for trade-offs with other key objectives (such as expanding population coverage and improving equity) given existing constraints. Importantly, each chapter provides an answer to pressing policy questions for informing resource allocation decisions in healthcare in LMICs. Below I highlight the unique contribution of each chapter and its limitations, and how these might be answered by future research.

Key contributions to the academic health economics literature are listed here. This thesis:

- enables, for the first time in all of the countries for which we provide estimates, the quantification of the likely health opportunity cost of funding decisions in healthcare, informing metrics of value (NHI and N$V) that reflect the scale of the benefits (or losses) that would be expected to result from decisions;
- demonstrates that the expected NHI of a healthcare intervention calculated using estimates of health opportunity cost in each country differs between countries and how tiered pricing could be used or, alternatively, the costs and benefits of applying a single price to all countries in terms of population health gains or losses;
- contributes to the evidence base required to appropriately account for the time streams of the health benefits and costs when conducting economic evaluations of healthcare interventions by providing estimates of the marginal cost per unit of health produced by the healthcare system over time for a range of LMICs $k_{i,t}$;
- develops an original framework which provides a means to inform answers to key questions in setting a HBP in a transparent manner that makes the best use of available data;

- and extends the framework to allow for the consideration of societal preferences for improvements in equity.

Further to making an original contribution to the academic health economics literature around opportunity costs, this work has also had real world impact in policy. This was made possible through close collaboration with decisionmakers within government and outside of government (e.g., non-governmental organizations which influence national decision-making) namely the Ministry of Health in Malawi and BMGF to identify the key questions for healthcare resource allocation in LMICs, which were then answered through the development and parameterising of frameworks to inform them. The reach of this impact extends to other governments and international organizations, with the early dissemination of the results from Chapter 2, which estimates of the marginal productivity of the healthcare system for 97 countries for 2015, influencing the WHO decision to formally step back from recommending the use of 1-3x GDP thresholds for decision-making in LMICs.[14,53] Chapter 3 responds to a policy need from the BMGF for methods to better inform funding priorities for the development of potential healthcare interventions.[38] Following the presentation of this work to members of executive board, the BMGF executive board used this analysis to inform the prioritization of product development decisions.[58] Chapter 4 of this thesis contributes to the evidence base required to apply the framework developed in Claxton et al (2019) [31] (not part of this thesis), which informs the Reference Case Guidelines for Benefit-cost Analysis in Global Health and Development, and has also been used by BMGF analysis to inform the prioritization of product development decisions.[58] Chapter 5 answers a direct request from the Ministry of Health in Malawi for analysis to inform the HSSP II, which includes designing a HBP for the country, and Chapter 6 extends this to transparently consider trade-offs between improving health and equity. In addition to informing Malawi's HSSP II, this work informed a review of the Ghanaian health insurance scheme, and has garnered interest from organizations and governments around the world involved in health benefits package design, and I have presented it to policy-making audiences in Latin America and Africa.

This work has limitations particularly surrounding the available data, which may be addressed by future research. The analysis on which Chapter 2 rests employs an IV approach to estimation to cross-sectional data, and models both public expenditure on health and a country's GDP as endogenous variables finding both a statistically and economically significant effect of public expenditure on health. Across the literature that evaluates this relationship findings are inconsistent, however, and a more robust approach to estimation would follow in the methodological and conceptual footsteps of existing within-country studies, summarised in Edney et al (2021) (not part of this thesis).[47] For this to be possible, countries need to expand data collection to enable analysis of variation in expenditure and outcomes over time and/or across geographical areas. The projections of $k_{i,t}$ estimated in Chapter 5 use pre-pandemic projections of GDP and should be updated when new projections of GDP are available. Chapter 6 uses international data on the costs and benefits of treatments at different coverage levels. It is hoped that this work stimulates more research into the data and analytic methods necessary

to inform the trade-offs inherent in UHC, which are not typically available despite their obvious value for informing decisions around the depth, breadth and height of coverage in LMICs. [686980]

The work in Chapter 5 demonstrates that using existing evidence can meaningfully inform key decisions in HBP design and resource allocation in healthcare; it also highlights areas where additional data would be valuable. One of these areas is data on how the costs and benefits (e.g., the latter in the case of interventions with dynamic effects, such as infectious diseases) of healthcare interventions differ depending on who among the population in need receives them. Another is the extent to which there are societal preferences for improvements in equity. Chapters 5 and 6 lay the groundwork for further methods development to support decision making in healthcare in LMICs, for example, around setting copayments, which may increase the scale of the budget for healthcare, but could reduce treatment-seeking behavior among those who need it, thus requiring careful consideration and having potential equity implications. Ultimately, the development of a dynamic, whole healthcare system model could inform of a wide range of critical decisions in resource allocation taking into account interdependence between healthcare interventions and the effects of health system strengthening interventions.

References

1.   Culyer, A. J. *Efficiency, Equity and Equality in Health and Health Care*. (2015).

2.   Ochalek, J., Revill, P. & Drummond, M. Allocating scarce resources-tools for priority setting. in *Global Health Economics: Shaping Health Policy In Low- And Middle-income Countries* 53–73 (World Scientific Publishing Co. Pte Ltd, 2020). doi:10.1142/9789813272378_0002.

3.   Drummond, M., Sculpher, M., Claxton, K., Stoddart, G. & Torrance, G. *Methods for the Economic Evaluation of Health Care Programmes*. (Oxford Medical Publications, 2015).

4.   WHO. *2015 Report of global survey on Health Technology Assessment by National Authorities*. (2015).

5.   NICE. Guide to the methods of technology appraisal. (2013).

6.   McCabe, C., Claxton, K. & Culyer, A. J. The NICE cost-effectiveness threshold: What it is and what that means. *Pharmacoeconomics* **26**, 733–744 (2008).

7.   Department of Health and Social Care. *DHSC Impact Assessment Example Report - Accelerated Access Collaborative for health technologies* .

8.   Pollard, C., Johnson, W. & Revell Ward, D. *Accelerated Access Collaborative - Improving Access to Digital Health Technology: Approvals, Reimbursement and Uptake*.

9.   Claxton, K. *et al.* Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess (Rockv)* **19**, 1–504 (2015).

10.   Ottersen, T. *et al.* A new proposal for priority setting in Norway: Open and fair. *Health Policy (New York)* **120**, 246–251 (2016).

11.   Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines. *Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines Final Report Final Report*. http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1449#purp (2019).

12.   Leech, A. A., Kim, D., Cohen, J. & Neumann, P. J. Use and Misuse of Cost-Effectiveness Analysis Thresholds in Low- and Middle-Income Countries: Trends in Cost-per-DALY Studies. *Value in Health* (2018) doi:https://doi.org/10.1016/j.jval.2017.12.016.

13.   *Making choices in health: WHO guide to cost-effectiveness analysis*. (World Health Organization, 2003).

14.   Bertram, M. Y. *et al.* Cost-effectiveness thresholds: pros and cons. *Bull World Health Organ* **94**, 925–930 (2016).

15.   Chi, Y.-L. *et al.* What next after GDP-based cost-effectiveness thresholds? *Gates Open Res* **4**, 176 (2020).

16.   Claxton, K. *et al.* Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold. *Health Technol Assess* **19**, 1–503, v–vi (2015).

17.   van Baal, P. *et al.* A cost-effectiveness threshold based on the marginal returns of cardiovascular hospital spending. *Health Econ* **28**, 87–100 (2019).

18.   Edney, L. C., Haji Ali Afzali, H., Cheng, T. C. & Karnon, J. Estimating the Reference Incremental Cost-Effectiveness Ratio for the Australian Health System. *Pharmacoeconomics* **36**, 239–252 (2018).

19.   Edoka, I. P. & Stacey, N. K. Estimating a cost-effectiveness threshold for health care decision-making in South Africa. *Health Policy Plan* **35**, 546–555 (2020).

20.   Siverskog, J. & Henriksson, M. Estimating the marginal cost of a life year in Sweden's public healthcare sector. *European Journal of Health Economics* **20**, 751–762 (2019).

21.   Stadhouders, N., Koolman, X., Dijk, C., Jeurissen, P. & Adang, E. The marginal benefits of healthcare spending in the Netherlands: Estimating cost-effectiveness thresholds using a translog production function. *Health Econ* **28**, 1331–1344 (2019).

22.   Vallejo-Torres, L., García-Lorenzo, B. & Serrano-Aguilar, P. Estimating a cost-effectiveness threshold for the Spanish NHS. *Health Economics (United Kingdom)* **27**, 746–761 (2018).

23.   Espinosa, O. *et al.* Estimating cost-effectiveness thresholds under a managed healthcare system: experiences from Colombia. *Health Policy Plan* **37**, 359–368 (2022).

24.   Chi, Y.-L. *et al.* What next after GDP-based cost-effectiveness thresholds? *Gates Open Res* **4**, 176 (2020).

25.   Ochalek, J., Lomas, J. & Claxton, K. Estimating health opportunity costs in low-income and middle-income countries: a novel approach and evidence from cross-country data. *BMJ Glob Health* **3**, e000964 (2018).

26.   Claxton, K., Ochalek, J., Revill, P., Rollinger, A. & Walker, D. *Informing Decisions in Global Health: Cost Per DALY Thresholds and Health Opportunity Costs*. (2016).

27.   Watkins, D. A. *et al.* Universal Health Coverage and Essential Packages of Care. in *Disease Control Priorities: Improving Health and Reducing Poverty* (eds. Jamison, D. T. et al.) (The International Bank for Reconstruction and Development / The World Bank, 2017). doi:10.1596/978-1-4648-0527-1/PT1.CH3.

28.   United Nations. Sustainable Development Goals. https://sustainabledevelopment.un.org/sdgs.

29. Arnold, M., Griffin, S., Ochalek, J., Revill, P. & Walker, S. A one stop shop for cost-effectiveness evidence? Recommendations for improving Disease Control Priorities. *Cost Effectiveness and Resource Allocation* vol. 17 Preprint at https://doi.org/10.1186/s12962-019-0175-6 (2019).

30. World Health Organization. *WHO Handbook for Guideline Development*. (World Health Organization, 2014).

31. Claxton, K. *et al.* Accounting for Timing when Assessing Health-Related Policies. *J Benefit Cost Anal* 1–33 (2019) doi:10.1017/bca.2018.29.

32. World Health Organization. Universal health coverage (UHC). https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc) (2021).

33. WHO. Universal coverage - three dimensions. *WHO* https://www.who.int/health_financing/strategy/dimensions/en/ (2015).

34. *What's In What's Out: Designing Benefits for Universal Health Coverage*. (Center for Global Development, 2017).

35. Giedion, Ú. *et al. Health Benefit Plans in Latin America: A Regional Comparison*. (Inter-American Development Bank, 2014).

36. *What's In, What's Out: Designing Benefits for Universal Health Coverage*. (Center For Global Development, 2017).

37. Ministry of Health. *Malawi Health Sector Strategic Plan 2011-2016*. (2012).

38. Bowie, C. & Mwase, T. Assessing the use of an essential health package in a sector wide approach in Malawi. *Health research policy and systems / BioMed Central* **9**, 4 (2011).

39. Ochalek, J. *et al.* Supporting the development of a health benefits package in Malawi. *BMJ Glob Health* **3**, e000607 (2018).

40. Ochalek, J. *et al.* Supporting the development of health benefits packages (HBPS): Principles and initial assessment for Malawi. in *Global Health Economics: Shaping Health Policy In Low- And Middle-income Countries* 265–273 (World Scientific Publishing Co. Pte Ltd, 2020). doi:10.1142/9789813272378_0010.

41. Manthalu, G., Nkhoma, D., Ochalek, J. M., Phillips, A. & Revill, P. Confronting tight fiscal, human resource, and evidence constraints, Malawi revises its benefits package | Request PDF. in *What's In, What's Out: Designing Benefits for Universal Health Coverage* (eds. Glassman, A., Giedion, U. & Smith, P. C.) 257–252 (Brookings Institution Press, Center for Global Development, 2017).

42.   Ochalek, J., Manthalu, G. & Smith, P. C. Squaring the cube: Towards an operational model of optimal universal health coverage. *J Health Econ* 102282 (2020) doi:10.1016/j.jhealeco.2019.102282.

43.   Palmer, S. & Raftery, J. Opportunity cost. *BMJ* **318**, 1551 (1999).

44.   Edoka, I. P. & Stacey, N. K. Estimating a cost-effectiveness threshold for health care decision-making in South Africa. *Health Policy Plan* (2020) doi:10.1093/heapol/czz152.

45.   Ochalek, J. *et al.* Informing a Cost-Effectiveness Threshold for Health Technology Assessment in China: A Marginal Productivity Approach. *Pharmacoeconomics* **38**, 1319–1331 (2020).

46.   Moler-Zapata, S. *et al.* Estimating the Health Effects of Expansions in Health Expenditure in Indonesia: A Dynamic Panel Data Approach. *Appl Health Econ Health Policy* (2022) doi:10.1007/S40258-022-00752-X.

47.   Edney, L. C. *et al.* Empirical Estimates of the Marginal Cost of Health Produced by a Healthcare System: Methodological Considerations from Country-Level Estimates. *PharmacoEconomics* 1–13 Preprint at https://doi.org/10.1007/s40273-021-01087-6 (2021).

48.   Gallet, C. A. & Doucouliagos, H. The impact of healthcare spending on health outcomes: A meta-regression analysis. *Soc Sci Med* **179**, 9–17 (2017).

49.   Feng, X., Kim, D. D., Cohen, J. T., Neumann, P. J. & Ollendorf, D. A. Using QALYs versus DALYs to measure cost-effectiveness: How much does it matter? *Int J Technol Assess Health Care* 1–8 (2020) doi:10.1017/S0266462320000124.

50.   Ochalek, J., Lomas, J. & Claxton, K. *Cost Per DALY Averted Thresholds for Low- and Middle-Income Countries: Evidence From Cross Country Data*. (2015).

51.   Ochalek, J., Lomas, J. & Claxton, K. Estimating health opportunity costs in low-income and middle-income countries: a novel approach and evidence from cross-country data. *BMJ Glob Health* **3**, e000964 (2018).

52.   Institute for Health Metrics and Evaluation. Global Health Data Exchange | GHDx. http://ghdx.healthdata.org/ (2022).

53.   Testimonial from former Economist, Department of Health Systems Governance and Financing, WHO. Preprint at (2020).

54.   Supplementary material for: Watkins, DA, DT Jamison, A Mills, R Atun, K Danforth, and others. 2018. "Universal Health Coverage and Essential Packages of Care." in *Disease Control Priorities: Improving Health and Reducing Poverty* (eds. Jamison, D. et al.) vol. 9 (World Bank, 2018).

55.   Malawi Ministry of Health. *Health Sector Strategic Plan II 2017-2022: Towards Universal Health Coverage*. http://www.health.gov.mw/index.php/policies-strategies?download=47:hssp-ii-final (2017).

56.   Vellekoop, H. Introducing rational healthcare prioritisation in Ghana: Methods and Challenges. in (Health Economics Research Centre (HERC), 2017).

57.   Mundel, T. Honing the Priorities and Making the Investment Case for Global Health. *PLoS Biol* **14**, e1002376 (2016).

58.   Testimonial from former Deputy Director of Data & Analytics, Bill and Melinda Gates Foundation. Preprint at (2020).

59.   Paulden, M., O'Mahony, J. & McCabe, C. Determinants of Change in the Cost-effectiveness Threshold. *Medical Decision Making* **37**, 264–276 (2017).

60.   Dieleman, J. L. *et al.* Future and potential spending on health 2015-40: Development assistance for health, and government, prepaid private, and out-of-pocket health spending in 184 countries. *The Lancet* **389**, 2005–2030 (2017).

61.   Edejer, T. T.-T. & Organization, W. H. *Making Choices in Health: WHO Guide to Cost-effectiveness Analysis, Volume 1*. (World Health Organization, 2003).

62.   Initiative for Vaccine Research of the Department of Immunization Vaccines and Biologicals. *WHO guide for standardization of economic evaluations of immunization programmes*. https://apps.who.int/iris/ (2019).

63.   Wilkinson, T. *et al.* The International Decision Support Initiative Reference Case for Economic Evaluation: An Aid to Thought. *Value Health* **19**, 921–928 (2016).

64.   Robinson, L. A. *et al. Reference Case Guidelines for Benefit-Cost Analysis in Global Health and Development*. https://sites.sph.harvard.edu/bcaguidelines/methods-and-cases/. (2019).

65.   Robinson, L. A., Hammitt, J. K., Jamison, D. T. & Walker, D. G. Conducting Benefit-Cost Analysis in Low- and Middle-Income Countries: Introduction to the Special Issue. *J Benefit Cost Anal* **10**, 1–14 (2019).

66.   Horton, S. Cost-Effectiveness Analysis in Disease Control Priorities, Third Edition. in *Disease Control Priorities in Developing Countries* (eds. Jamison, D. T. et al.) (The World Bank, 2017).

67.   Vellekoop, H., Odame, E. & Ochalek, J. Supporting a review of the benefits package of the National Health Insurance Scheme in Ghana. *Cost Effectiveness and Resource Allocation 2022 20:1* **20**, 1–14 (2022).

68. Surgey, G. *et al.* Introducing health technology assessment in Tanzania. *Int J Technol Assess Health Care* **36**, 80–86 (2020).

69. Schmitt, L. *et al.* Concomitant health benefits package design and research prioritisation: development of a new approach and an application to Malawi. *BMJ Glob Health* **6**, e007047 (2021).

Abbreviations

BCA	benefit cost analysis
BMGF	the Bill and Melinda Gates Foundation
CEA	Cost-effectiveness analysis
CHE	Centre for Health Economics
DALYs	Disability Adjusted Life Years
DCPN	the Disease Control Priorities Network
EHP	essential health package
Gavi	Gavi, the Vaccine Alliance
GBD	Global Burden of Disease
GCEA	generalized cost effectiveness analysis
GDP	gross domestic product
The Global Fund	The Global Fund to Fight AIDS, Tuberculosis and Malaria
HBP	health benefits packages
HSSP	Health Sector Strategic Plan
HIC	high-income country
HPV	human papillomavirus
HTA	health technology assessment
ICER	incremental cost effectiveness ratio
iDSI	the International Decision Support Initiative
IV	instrumental variable
LMIC	low- and middle-income countries
MoH	Ministry of Health
N$V	net dollar value
NCI	net consumption impact
NHI	net health impact
NHS	National Health Service

NICE   National Institute for Health and Care Excellence

NoMA   Norwegian Medicines Agency

NPV   net present value

ODI   Overseas Development Institute

QALY   quality-adjusted life year

UHC   Universal Health Coverage

UN   the United Nations

WHO-CHOICE WHO-CHOICE (CHOosing Interventions that are Cost-Effective) initiative

YLD   years of life disabled

YLL   years of life lost

Appendices

Appendix 1. Letter from MoH Malawi

Appendix 2. Published papers

Appendix 1. Letter from MoH Malawi

Fax No. : 01 789 365
Communications Telephone
No. Lilongwe - 01 789 400
Should be addressed to
Secretary for Health

In reply please quote No. ....

MINISTRY OF HEALTH
PRIVATE BAG 30377
CAPITAL CITY
LILONGWE 3

Ref. No. DPPD/27

2nd February 2017

Ms. Jessica Ochalek
Centre for Health Economics
University of York
YO10 5DD
Heslington
York
United Kingdom

Dear Madam,

VOTE OF THANKS

We would like to sincerely thank you for your technical support in the revision of our essential health care package (EHP).

It has been a long road since March 2016 but we are now at a place where a draft basic health care package is in place and it is being discussed by stakeholders. This is down to, in a great part, your hard work and commitment in developing a guide and tool for this process.

We acknowledge the visits you made to get a first-hand understanding of the context as well as the remote support you provided. Colleagues in the Department of Planning and Policy Development rate the EHP report as one of the best technical documents that have been produced for the Ministry.

I wish you great success in your career.

Yours Sincerely,

Gerald Manthalu, PhD
For: **SECRETARY FOR HEALTH**

Appendix 2. Testimonial from former Economist, WHO Department of Health Systems Governance and Financing, November 2020

University of Strathclyde

199 Cathedral Street

Glasgow, G4 0QU

+44(0)7810 754 023

jeremy.lauer@strath.ac.uk

27 November 2020

Dear Professor Claxton,

I am writing in support of your Impact Case on Global Health Budget Allocation, specifically the impact your team's research has had on WHO guidance and policy.

I am the Director of Research and Professor in the Department of Management Science at Strathclyde University. Prior to taking up my appointment at Strathclyde in February of this year, for 25 years I was an Economist at the World Health Organization (WHO) where I was closely associated with WHO's work on priority setting and economic evaluation (WHO-CHOICE). I have known and worked closely with you and your colleagues at the Centre for Health Economics (CHE) and the Department of Economics at the University of York. The research detailed in your Impact Case has been instrumental in shifting thinking about economic evaluation at the WHO, not only through direct collaboration with staff in a number of WHO programmes but also through sustained strategic dialogue with key WHO staff in the economics and health financing department, of which I was formerly a member.

Globally, health budgets are formulated in a complex environment, and this particularly so in low- and middle-income countries (LMICs), which face multiple constraints. The research done by you and your colleagues at the Centre for Health Economics and the Department of Economics demonstrated in particular that the way in which cost-effectiveness thresholds were being used was not appropriate to the environment in which decision-makers in LMICs operate.

In 2001, the WHO's Commission on Macroeconomics and Health had suggested that interventions could be considered 'cost-effective' if the resources required for their implementation cost less than 3 times GDP per capita per DALY averted. In the years following, staff at WHO and many external researchers adopted this threshold as a *de facto* guideline, i.e. for the purpose of recommendations about national-level decision-making. The innovative research done at York showed, however, that the actual threshold for many LMICs would often be much lower than 1 times GDP per capita, and that using the higher threshold of 3 times GDP implied getting much less value for money from public spending on health.

This research directly influenced a series of decisions at WHO to clarify its position about cost-effectiveness thresholds for LMICs. This then catalysed a generalized move away from the prevailing fixation on idealized demand-side benchmarks and enabled in turn the increased prioritization and scale-up of interventions that could deliver higher health gains for lower cost. Whereas many previous cost-effectiveness studies routinely cited the Commission's threshold,

most published studies now try to ascertain the opportunity costs of existing budgetary commitments, thereby rationalizing the use of economic evaluation in decision-making. This can in particular be seen in the use of health technology assessment in LMICs, where York's research has had a major impact.

The research done at York at the Centre for Health Economics also had a significant influence on WHO's clinical guidance and treatment guidelines, particularly with reference to HIV/AIDS. In previous years, such guidelines did not take into account the results of the economic evaluation of spending priorities; however, following a number of seminars and workshops conducted in Geneva to discuss York's research, the WHO HIV Treatment Guidelines now place a much greater priority on economic criteria.

The WHO continues to work closely with you and your colleagues, for example through the Centre for Global Development's Working Group on Goals and Guidelines, and I expect that valuable economic insights from York will continue to inform global health policy for the foreseeable future.

Warm regards,

Jeremy A. Lauer, Ph.D.
Professor and Director of Research
Department of Management Science
Strathclyde University
Glasgow, United Kingdom
and
(formerly) Economist
World Health Organization
Geneva, Switzerland

Appendix 3. Testimonial from former Deputy Director of Data & Analytics, Bill and Melinda Gates Foundation, November 2020

Damian Walker
735 35th Ave, Seattle, WA 98122 USA
+1 206 658 5122
damiangwalker@gmail.com

Research Excellence Framework: statement supporting impact for Professor Karl Claxton, University of York, UK

Informing Decisions in Global Health: Cost Per DALY Thresholds and Health Opportunity Costs

30 November 2020

To whom it may concern

I am writing in support of the above research which made and continues to make significant contributions to people's health through its use at the Bill & Melinda Gates Foundation, and among its partners.

Between 2010 and 2015 I was Senior Program Officer for Cost-Effectiveness, and between 2016-2019 Deputy Director for Data and Analytics, at the Bill & Melinda Gates Foundation. As such, during the last decade I had primary responsibility for developing the foundation's first strategy for economic evaluation in health and development. This involved defining standards for how studies should be conducted and reported, resulting in "references cases" for both cost-effectiveness analysis and benefit cost analysis. I also funded the Tufts Global Health Cost-Effectiveness Registry, to ensure that the evidence generated on the cost-effectiveness of interventions was collated, regularly updated, standardized, and easily accessible to all. The third and final pillar in my strategy was to build and support institutions and processes to use cost-effectiveness evidence. This led to the creation of the International Decision Support Initiative (or iDSI), building on the early success of NICE International.

In addition to my work making and managing grants, I helped conceive, pilot and launch an internal health technology assessment process at BMGF – the Integrated Portfolio Management (or IPM) tool and process – which supports more than 100 health products at various stages of R&D.

The grants and contracts I made to Professor Claxton between 2014-2019 contributed directly and indirectly to our work on the economic evaluation of global health. Internally, Professor Claxton's estimates of health opportunity costs in low- and middle-income countries contributed to the foundation's precision public health approach. However, arguably, Professor Claxton's work made a greater contribution among and through our partners. For example, his methods and applied research influenced the World Health Organization's disavowal of their crude 1-3 times GDP thresholds. The work, and other York research on how uncertainty and the need for evidence should be assessed, also contributed to the iDSI reference case, and consequently influenced hundreds of applied economic evaluations, as well as numerous national HTA guidelines, e.g. Indonesia and Malawi. I was also struck at how the work advanced the work of some of our major grantees working in this space. For example, the Disease Control Priorities project embraced the approach and preliminary estimates to refine the design of their recommended health benefit packages for low- and middle-income countries. For too many years, the theory and methods of economic evaluation in health care had been siloed between

practitioners in high-income countries, and those in low- and middle-income countries. Professor Claxton's work provided a much needed "bridge" between these two epistemic communities.

In summary I am grateful for the contributions of Professor Claxton and his team to the application of economic evaluation methods in low- and middle-income countries. While it is impossible to quantify the size of these contributions in terms of lives saved, his team should be recognized for their contributions toward better decisions that have undoubtedly led to better health.

Sincerely,

Damian Walker

Currently Non-Resident Fellow, Center for Global Development
Previously (2010-2019), Deputy Director of Data & Analytics at the Bill & Melinda Gates Foundation

Appendix 4. Published papers

Appendix 2.1: Ochalek J, Lomas J, Claxton K.P., *Estimating health opportunity costs in low- and middle-income countries: a novel approach and evidence from cross-country data*, <u>BMJ Global Health</u>, 3(6), 2018. <u>http://dx.doi.org/10.1136/bmjgh-2018-000964</u>

Appendix 2.2: Ochalek, J. M., Abbas, K., Claxton, K. P., Jit, M. & Lomas, J., *Assessing the value of human papillomavirus vaccination in Gavi-eligible low- and middle-income countries*, <u>BMJ Global Health</u>, 2020 Oct 20, 5:e003006. <u>http://dx.doi.org/10.1136/bmjgh-2020-003006</u>

Appendix 2.3: Lomas, J., Claxton, K., Ochalek, J., *Accounting for country- and time-specific values in the economic evaluation of health-related projects relevant to low- and middle-income countries*, <u>Health Policy and Planning</u>, 2021;, czab104, <u>https://doi.org/10.1093/heapol/czab104</u>

Appendix 2.4: Ochalek, J. M., Revill, P., Manthalu, G., McGuire, F., Nkhoma, D., Rollinger, A., Sculpher, M.J., Claxton, K. P., *Supporting the development of a health benefits package in Malawi,* <u>BMJ Global Health</u>, 3(2), 2018. <u>http://dx.doi.org/10.1136/bmjgh-2017-000607</u>

Appendix 2.5: Ochalek J., Manthalu, G., Smith, P.C., *Squaring the cube: Towards an operational model of optimal universal health coverage*, <u>Journal of Health Economics</u>, 2020 Mar, 70(102282). doi: <u>https://doi.org/10.1016/j.jhealeco.2019.102282</u>