

# **Economic evaluation and equity impact analysis of interventions for maternal and child health in Tanzania**

Evidence for fair and efficient priority setting

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## **DEDICATION**

I dedicate my dissertation to my wife Dr Frida Namnyak Ngalesoni for her endless love, support, commitment and tenacity during the entire doctorate period. You are the greatest gift of my life. To our wonderful brood, daughter Gabriella Byera and son Jayden Baraka, you have been brave, travelling miles around the continent and coping with our absence from time to time. Thank you for being good. You always provided me with something to cheer me up.

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## **Scientific environment**

The PhD project was undertaken while I was a member of the research group Global Health Priorities at the Department of Global Public Health and Primary Care, Faculty of Medicine and Dentistry, University of Bergen.

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## **Abstract**

### **Introduction**

Tanzania has seen a progressive decline in maternal and child mortality over the years. The last two decades have been a landmark with about 50% reduction in maternal and child mortality. However, the recorded improvements in the health status of mothers and young children in Tanzania is masked by geographical variation in the reduction of maternal and child mortality. In 2010, the under-five mortality in the Lake zone was reported to be 109 deaths per 1000 live births compared to the Northern zone where it was 58 deaths per 1000 live births. Key interventions addressing maternal and child health problems are inequitably distributed. There is a 57% difference in maternal mortality between poor and rich pregnant women. Similar trends are observed in interventions which address health problems in children under-five, though to a lesser magnitude with a gap of 10% to 15% between poor and rich populations. Economic evaluations of interventions for maternal and child health are imperative in generating evidence and informing context-specific allocation decisions to achieve rapid reductions in maternal and child mortality.

The aim of the study is to generate evidence on a selection of maternal and child health interventions so this can inform priority-setting decisions in the direction of increased coverage for effective interventions that improve health outcomes and redress inequity.

### **Methods**

The health system implementation costs, including programme costs, were quantified to calculate the cost-effectiveness of adding rotavirus and pneumococcal vaccines to the Expanded Programme on Immunisation. The costs for the provision of diarrhoea and pneumonia treatment to children were quantified. We employed the ingredient and step-down costing approaches for the analysis of costing data. The cost and coverage data were collected from one urban and one rural district hospital and a health centre in Tanzania in 2012. Secondary data on disease epidemiology, national level intervention coverage and effects were retrieved from published literature and

government reports. We used DALYs, QALYs and LY as the outcome measures and estimated incremental costs and health outcomes using a Markov model. For the equity impact analysis we used the Lives Saved Tool (LiST) to estimate potential reductions in maternal and child mortality and the number of lives saved across wealth quintiles and between rural and urban settings.

## **Results**

The introduction of rotavirus vaccine alongside the current diarrhoea treatment is highly cost-effective compared to diarrhoea treatment given alone, with incremental cost-effectiveness ratio (ICER) of US\$ 112 per DALY averted. The 13-valent pneumococcal vaccine is cost-effective, with ICERs of 258 per QALY gained and US\$ 245 per LY gained for Tanzanian settings, compared to no vaccine and 10-valent pneumococcal vaccine. However, the differences between pneumococcal vaccines were not robust with scenario analyses. Varying key model parameters may switch the results in favour of either of the pneumococcal vaccines. The probability of being cost-effective for both vaccines was at a much lower level than willingness-to-pay for health of US\$609 per capita Tanzania gross domestic product (GDP). It is probable that using both vaccines is highly cost-effective at a price far below a willingness to pay for health of US\$609 per capita Tanzania's gross domestic product.

The scale up of key, highly cost-effective interventions is likely to save more than twice as many mothers and children under five in the poorest population quintiles compared to the richest quintile in Tanzania. Increasing intervention coverage to equal levels across quintiles would also reduce inequalities in maternal and child mortality.

## **Conclusion**

This study has shown that it is possible to use currently available methods and tools to generate evidence for policy decisions in low-income settings. Combining available information on the burden of disease, economic evaluation and equity analysis to develop evidence-based health policies and plans to ensure fair and efficient resource allocation is possible, but remains a challenge. The use of scientific evidence is an important element in informing both policy and prioritisation decisions

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about health interventions. Health policy developed on the basis of systematically generated evidence is likely to be acceptable and achieve the goals of universal access to health services regardless of need.

## List of publications

### Paper I

Ruhago G, Ngalesoni F, Robberstad B, Norheim O. Cost-effectiveness of live oral attenuated human rotavirus vaccine in Tanzania. *Cost-Effectiveness and Resource Allocation*. 2015;13(1):7.

### Paper II

Ruhago G, Ngalesoni F, Robberstad B, Norheim OF. Cost effectiveness of universal pneumococcal vaccination in Tanzania: Pharmacoeconomic evaluation of 10 valent and 13 valent vaccines. [Under Review].

### Paper III

Ruhago, G.M., F.N. Ngalesoni, and O.F. Norheim, Addressing inequity to achieve the maternal and child health millennium development goals: looking beyond averages. *BMC public health*, 2012. **12**(1): p. 1119.

## 1.0 Introduction

### 1.1 Maternal and child health in Tanzania

Health policy addressing maternal and child health in Tanzania dates back to the post-independence era in the 1960s (see Table 1). In 1967, the first national agenda for the transformation of socioeconomic development was proclaimed, popularly known as the Arusha declaration. The focus in the health sector was on changing national health priorities from a major emphasis on curative services to preventive services and health promotion, a move towards training low cadre health workers to serve in primary health care and rural areas. The Maternal and Child Health Committee was established at the Ministry of Health and Social Welfare in 1971, followed by the launch of the countrywide Maternal and Child Health (MCH) Services in 1974, providing vaccination, antenatal and post-natal services, growth monitoring and treatment of minor health problems among pregnant women and children under five [1, 2].

The global economic crisis in the 1980's led to changes in development and economic policies in Tanzania, through the Economic Structural Adjustment Programs (ESAP) proposed by the Bretton Wood institutions [3]. Reforms in the delivery of social services were introduced e.g. reduction of government expenditure on health and education and retraction of civil servants including health workers [4]. Consequently the health sector was affected and many achievements in the sector gained since independence were reversed [5]. In response to worsening population health and quality of health care following the ESAP, the government introduced health sector reforms in the mid 1990's [6]. Government health care financing had dropped dramatically [3, 7]; alternative sources for financing health care apart from the central government budget allocations were initiated. A cost-sharing strategy was introduced: patients seeking health care services in public health facilities were to contribute by paying a user fee to cover part of the health care costs. The fee amount is determined by the local health facility board, and then approved by either district or regional health management teams depending on the level of the system the health

care intervention in question belongs to. The district and regional boards approve user fees for primary and secondary health care facilities. The fees for tertiary health facilities are set by the hospital board and approved by the Ministry of Health. To reduce the work load on overburdened public services, and to increase access to health care, the government promoted private sector investment in health care services. The private health services include faith-based and private not-for-profit health providers, where the government bears part of the costs, such as health workers' salaries, drugs and medical supplies. Private-for-profit services were allowed, after previously being abolished. In these private services, all costs are borne by the patient either through out-of-pocket payments or health insurance. Further reforms involved decentralization through devolution from central to local government. The mandate of planning and implementation of priority health intervention was placed upon districts through District Health Management Teams (DHMT) [8]. Above and beyond the reforms listed above, health care services were made free for pregnant women, children under five and poor households.

In the last decade, health policy has evolved continuously, with the implementation of a national package of Essential Health Interventions and the Health Sector Strategic Plan II (2003-2007). These have focused on the provision of quality health services through the Essential Health Package (EHP) targeting basic health care services to maximise the use of limited resources. Again, essential interventions for maternal and child health are prioritized [9, 10]. Currently the Health Strategic Plan III (2009-2015), alongside its sister programme, the Primary Health Services Development Programme (2007-2017) are under implementation [11, 12]. The key aim of these strategies is to enhance partnership between government ministries, departments, agencies and development partners in the implementation of activities to achieve the health-related Millennium Development Goals (MDG). The attainment of maternal and child health related MDGs 4 and 5 is strongly emphasised in these documents.

**Table1: Maternal and child health policy paper in Tanzania**

Year	Policy/initiative	Priorities/Goal
1971	Maternal and child health committee	Young children protection
1974	MCH Strategy	To provide mothers and young children with immunisation, nutrition education, antenatal and post-natal care, treatment of minor health problems, growth and monitoring
1975	Expanded Programme on Immunisation	Immunization of all vaccine-preventable childhood illness
1989	Safe Motherhood Initiative	Reduction of the burden of maternal mortality and morbidity
1990	National Health Policy of 1990	Reduction of maternal and child mortality through provision of equitable maternal and child health services
1992	National Population Policy	To strengthen accessibility of family planning services so as to reduce maternal and child mortality
1992	Baby-friendly Hospital Initiative	Transforming maternity facilities into centres for breastfeeding support
1994	The Code of Marketing Breast Milk Substitutes	To provide education and information about infant and young child feeding and protect women against misinformation
1996	Integrated Management of Childhood Illness (IMCI)	Integrated approach to child health by improving case management skills of health care staff, overall health systems and improving family and community health practices.
1997	Strategy for Reproductive Health and Child Survival	Improving the health of women, children, and adolescents.
2000	Tanzania national Package of Essential Health Intervention	The package includes provision for reproductive and child health interventions such as antenatal care, care during child birth, emergency obstetric care (EmOC), immunisation, IMCI and family planning
2003	The National Policy Guidelines for Reproductive and Child Health Services	Integration of HIV and AIDS services into reproductive health and family planning services, including provision of health education, HIV screening and testing, and Prevention of Mother to Child Treatment (PMTCT)
2004	Tanzania's National Guidelines on Prevention of Mother-to-Child Transmission of HIV (PMTCT)	Reduction of mother-to-child transmission of HIV and to improve care for infected parents and children by introducing and scaling up comprehensive PMTCT services within all RCH facilities.
2005	National Strategy on Infant and Young Children Feeding and Nutrition	Underpins the importance of exclusive breastfeeding and other infant and young child feeding practices
2005	Reproductive and Child Health Strategy 2005-2010	To provide quality of reproductive and child health services including antenatal care, skilled birth attendants and post-partum care, Provision of care for obstetric emergencies, post-abortion care and family planning,
2007	National Health Policy of 2007	Free health services to pregnant women and children under five, provision of quality health of MNCH services,
2007	The Primary Health Care Services Development Programme 2007- 2017	To reduce maternal mortality ratio from 578 to 220 per 100,000 live births through provision of basic and comprehensive obstetric care including emergency care; provision of ambulances, motor cycles to targeted health facilities to facilitate outreach services. Provision of equitable and all-time-accessible health services in every village
2007	Tanzania's National Guidelines on Prevention of Mother-to-Child Transmission of HIV (PMTCT), 2007, revision of 2004 Guideline	Reduction of mother-to-child transmission of HIV and to improve care for infected parents and children by introducing and scaling up comprehensive PMTCT services within all RCH facilities.
2008	The National Road Map Strategic Plan, to accelerate reduction of maternal, new born and child deaths in Tanzania 2008 - 2015	To strengthen and coordinate the delivery, maternal, new born and child health interventions across the continuum of care i.e. the delivery of MNCH life-saving interventions as a package.
2013	National Guidelines for Comprehensive Services for Prevention of Mother-to-Child Transmission of HIV and Keeping Mothers Alive (PMTCT) (Revision of the 2007 Guideline)	Change from 2007 guideline to Option B+

Sources [10, 12-18]



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## 1.2 Maternal and child health status

Tanzania has seen a progressive decline in maternal and child mortality over the years. The last two decades have been a landmark with about 50% reduction in maternal and child mortality. According to the 2014 World Health Organization (WHO) health statistical report, mortality in children under five has been reduced from 158 deaths per 1000 live births in 1990 to 68 deaths per 1000 live births in 2011. However over 50% of the under-five mortality occurs before the first birthday: infant mortality is 45 deaths per 1000 live births. Maternal mortality has dropped from 910 in 1990 to 410 in 2011 per 100,000 live births [19, 20]. Comparing the progress against the neighbouring east African countries as a benchmark, Tanzania fares well ahead of Kenya and Uganda.

However, the recorded improvements in the health status of mothers and young children in Tanzania mask geographical divergence in the reduction of maternal and child mortality. In 2010, the Lake zone under-five mortality was reported to be 109 deaths per 1000 live births compared to the Northern zone 58 deaths per 1000 live births [21]. Key interventions addressing maternal and child health problems are inequitably distributed. There is a 57% difference in maternal mortality between poor and rich pregnant women. As many as 90% of women in rich communities have births attended by a skilled health worker compared to only 33% of the poorest populations. Similar trends are observed in interventions addressing health problems in children under five, though to a lesser extent, with a gap of 10% to 15% between the poor and the rich population [21].

The lack of progress in addressing geographical and socioeconomic differences in maternal, neonatal and child mortality rates jeopardises the chances of achieving the MDGs. The inequitable distribution of maternal and child health outcomes is also contrary to the main aim of national health policy which states explicitly that, “*the policy will aim at providing basic health services that are geographically accessible to all people, of good quality, affordable and sustainable*”[16]. To ensure equitable reduction in diseases, disabilities and deaths especially in women and children it is

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crucial that evidence-based interventions addressing geographical and socioeconomic inequalities are implemented nationwide with guaranteed equal access to all.

### 1.3 Implementation of maternal and child health policy

The Essential Package of public health and clinical services was proposed in 2000 as a guiding document to be used in implementing health policies and strategies, to ensure efficient resource use and universal coverage of health care services [22]. The Essential Package is meant to define what clinical and preventive services will be offered and on what scale and, therefore, invariably dictates the context-specific health care priority setting [23]. The Tanzania Essential Health Package has expanded rapidly in the last ten years. On its inception early in the 2000's, the package had only five priority areas [10]. Currently, since 2011, it includes thirteen priority areas with over 200 interventions, refer to (Table 2) [24]. The defined priorities are quite broad including disease conditions, medical equipment, physical infrastructure, and so on [24]. While it may be possible to reallocate resources within priority areas, in its current form the Essential Package does not provide sufficient information to allow trade-off between priority areas. The criteria used to include or exclude interventions in the package are not clearly elaborated. It is only mentioned that the package will include interventions that are cost-effective and address the major burden of disease [10, 24]. However, no information is provided about the methods or the institutional structure responsible for overseeing inclusion and exclusion of interventions in the Package.

Inconsistency in the use of evidence to set national health priorities jeopardises efficiency and may lead to inequitable distribution of health services. A recent mid-term review of the implementation of the Health Sector Strategic Plan III has indicated the existence of inequitable geographical access to health care services. The number of health facilities has increased nationally but these are inequitably distributed. In Kagera, a predominantly rural region, only 25% of the population live within 5km of a health facility compared to the urban Dar es Salaam region which

has 100% coverage [25]. The areas reported to have the low coverage of health services have also shown poor maternal and child health outcomes [21].

Economic evaluations of interventions for maternal and child health are imperative in generating evidence and informing context specific allocation decisions to achieve rapid reductions in maternal and child mortality. It has been suggested that cost-effectiveness and equity impact analysis, coupled with explicitly fair processes of setting health care priorities may be helpful in redressing inequality and improving health outcomes [26].

**Table 2: The Tanzania National Essential Health Package: Priority interventions**

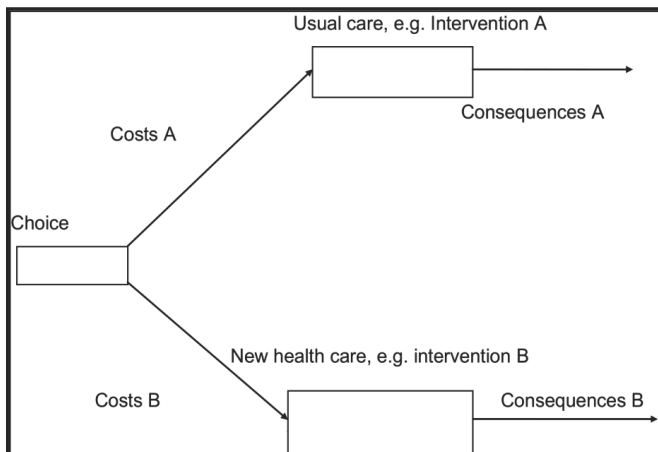
No	Priority area
<b>The 2000 EHP</b>	
1	Reproductive and child health
2	Communicable disease control
3	Non-communicable disease control
4	Treatment and care of other common diseases of local priority within the district
5	Community health promotion and disease prevention
<b>The 2011 EHP</b>	
1	Medicines, medical equipment, medical and diagnostic supplies, management systems
2	Maternal, new born and child health
3	Communicable diseases
4	Non – communicable disease control
5	Treatment and care of other common diseases of local priority within the Council
6	Environmental health and sanitation
7	Strengthen social welfare and social protection services
8	Strengthen human resources for health and social Welfare Management Capacity for improved health services delivery
9	Strengthen organizational structures and institutional management at all levels
10	Emergency preparedness and response
11	Health Promotion/ Behaviour Change Communication (BCC)
12	Traditional medicine and alternative healing
13	Construction, rehabilitation and planned preventive maintenance of physical infrastructures of health facilities

Source [10, 24]

## 2.0 Economic evaluation in health care

### 2.1 What is health care economic evaluation?

Economic evaluation is a comparison of alternative health care interventions in terms of their cost (input) and outcomes (outputs) [27]. Costs are values of resources used in providing the intervention, for example, health care cost or costs incurred by the patient or family e.g. transport or wages lost because of illness. The outcomes are the health effects of the interventions being compared e.g. Life Year (LY) saved, Disability Adjusted Life Years (DALYs) or Quality Adjusted Life Years (QALYs). There may be other types of outcomes, such as those relating to process (e.g., cases found) [28]. Economic evaluations in health care rest on the premise that all resource use involves some opportunity cost; that is, scarce resources could be put to some alternative best use [27].



Source [27]

**Figure 1: Simple illustration of an economic evaluation design**

Health care economic evaluation consists of several steps such as identification, measurement and valuation of costs and consequences. The process includes defining the question to be addressed in the study e.g. will the new intervention produce extra health outcomes compared to alternatives? The process also involves describing the perspective or viewpoint from which the study will be conducted, ie, is it a narrow

focus concerned with the costs and consequences of interest to the provider or does it include a societal perspective where all costs and consequences are considered, regardless of who bears them?

A full economic evaluation includes all possible alternatives, e.g. usual care, compared to a new intervention (Figure 1) or compared with the “do nothing” or null scenario, whereby interventions are compared to a state where the individual would receive no health care intervention, as proposed in generalised cost-effectiveness analysis [27-30]. Economic evaluation involves the following key steps: defining the study question and the type of economic evaluation suitable to answer the question; identifying and measuring costs of resources used in delivering the study interventions; the health outcome measure suitable for the study e.g. DALYs or QALYs, etc.; exploring uncertainties surrounding parameters used in the evaluation; and examining the distributional impact of the economic evaluation results.

## 2.2 Types of economic evaluation

The type of health care economic evaluation depends on the question to be addressed, the alternatives being evaluated, and the outcomes of interest. There are four types of economic evaluations commonly used (summarised in table 3 below) [27-29]:

<b>Table 3. Measurement of costs and consequences in economic evaluation</b>			
<b>Type of study</b>	<b>Measurement /valuation of costs in both alternatives</b>	<b>Identification of consequences</b>	<b>Measurement/valuation of consequences</b>
Cost analysis	Monetary units	None	None
Cost-effectiveness analysis	Monetary units	Single effect of interest, common to both alternatives, but achieved to different degree	Natural units (e.g. life years gained, disability days saved, points of blood pressure reduction, etc.)
Cost-utility analysis	Monetary units	Single or multiple effects, not necessary common to both alternatives	Healthy life years (typically measured as Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs))
Cost-benefit analysis	Monetary units	Single or multiple effects, not necessarily common to both alternatives	Monetary units

Source: [27]

### **2.2.1 Cost of illness or cost-minimisation analysis (CMA)**

The alternative interventions in CMA are assumed to have equivalent effectiveness or consequence and so only cost is analysed and reported. This type of evaluation is mainly conducted alongside clinical trials and reported when the trial does not reveal significant differences between interventions. The application of CMA in economic evaluation is currently limited since the uncertainty around the effectiveness is an important part of economic evaluation

### **2.2.2 Cost-effectiveness analysis (CEA)**

Cost and effects of the alternative interventions are calculated and presented as difference in cost (denominator) per difference in a single unit of outcome (numerator), e.g. reduction in diarrhoea episodes, LY gained etc.

### **2.2.3 Cost-utility analysis (CUA)**

This form of economic evaluation has similar methods to CEA, except the outcome measures, which combine mortality and morbidity into a single generic measure e.g. QALYs gained or the DALYs averted. In most literature the two measures CEA and CUA are used interchangeably. Throughout this thesis we will use the term CEA.

### **2.2.4 Cost-benefit analysis (CBA)**

This type of economic evaluation expresses health outcomes in monetary values using various techniques e.g. human capital approach and willingness-to-pay methods. The additional benefit of CBA is that it allows for comparison of interventions across different sectors. However its application in health care is challenged by the technical and ethical difficulties of placing a monetary value on health outcomes.

## **2.3 Costing health care services**

Costing in economic evaluations is based on the concept of opportunity costs. This involves identifying what resources are involved in delivering the intervention,

measuring the amount of each resource involved, and valuing each resource at the level of its best alternative use. This implies applying economic value to the resources (replacement cost), rather than accounting or financial cost (the acquisition price). For example, the cost of volunteer workers will not appear in financial accounting, but when applying the principle of opportunity cost, the volunteer workers' time will be valued as the equivalent to the cost of hiring personnel with similar qualifications [30]. A similar approach is applied to donated goods.

Costing in health care is influenced by the study perspective, which determines the source of resources. Generally there are two main perspectives, (1) the provider perspective, where only health care providers are considered e.g. staff, administration costs, equipment and buildings and (2) the societal perspective, where all costs are relevant e.g. the resources used by the health care provider, from primary to tertiary levels, costs incurred by patients/families, other parties in society e.g. insurance companies, donors, etc.

The resources used in providing and consuming health care services can be categorized into direct and indirect costs. The direct costs are resources used in providing health care services such as health personnel, drugs, medical equipment etc. The indirect costs are resources used by the patient and family seeking health care and the associated loss in productivity. These include travel costs, care provided by family, the loss of work time and consequent productivity loss. Costs to the patients and family can be estimated using methods such as the human capital approach, which estimates loss of earning or productivity loss during the period of illness; or the friction cost method, which only estimates productivity loss before the employer makes a replacement. The methods are explained in detail elsewhere [28, 31]. The resources use can be classified into fixed and variable resources. The use of fixed resources is constant irrespective of the output such as buildings, some medical equipment (e.g. X-ray machines, CT scanners). The use of variable resources such as staff, drugs, or laboratory reagents changes with the output e.g. number of patient attended at outpatient department or number of tests in the laboratory.

There are several approaches to costing health care services. Resource use may be estimated using expenditure records, or the ingredient approach can be used. The latter is mostly applied in costing for economic evaluations [30]. In the ingredient method, all departments involved with the intervention are defined and the resources inputs used to deliver the intervention in each department are enumerated and assigned cost. The cost from each department is then combined to obtain the total cost of delivering the intervention [32, 33]. Most costs in a health care facility are shared in delivering different interventions. The application of the step-down costing approach enables the distribution of the shared costs [27, 31].

### **2.3.1 Identifying resource use**

This stage seeks to identify the resources required for the intervention. To enable accurate identification of all resources, departments are divided into cost centres. The input and expected output are then defined in each cost centre [32, 34]. The cost centres may be distinguished into three levels: first the direct cost centres, which provide treatment services to the patient e.g. outpatient clinics or inpatient wards; second the intermediate centre, which provides health care services, but not direct treatment of the patient e.g. pharmacy and laboratory services; and finally the indirect services, which provide support services to the first two tiers, such as, security, laundry and administration [34].

Input resources are then divided into two main categories, recurrent and capital goods. Recurrent resources are inputs with a lifespan of one year or less e.g. employee wages, stationery, drugs etc. The recurrent input resources may be identified from duty rosters or wage bills, order books, store ledgers, or accounts records such as receipts etc. Capital resources involve inputs which have a life span of more than one year, for example, buildings, equipment, cars etc. Capital items can be identified from health facility inventories, physical counting in each department etc. Output resources may be the number of children vaccinated or the number of pregnant women who attended Maternal and Child Health Clinics.



### 2.3.2 Resource measurement

Once resources have been identified they need to be measured. This involves being able to attribute the exact resource use for each intervention and quantifying the total resources used by each service centre. These are generally measured in some sort of physical unit, e.g. the amount of doctor's time, the amount of a drug used, the number of tests consumed, building space used etc.

Decisions are needed when dealing with resources shared across a number of interventions. For example, to allocate resources to a specific intervention within an inpatient ward or to allocate clinician time per patient, some appropriate factor has to be used, such as the number of bed days for each diagnosis. The step-down costing method has been used to allocate shared costs across health care services. Detailed worked examples are provided elsewhere [27, 31, 34].

### 2.3.3 Resource valuation

All individual units identified in the measurement process have to be assigned corresponding costs. The prices can be obtained from different sources, for example in Tanzania, up to date prices for drugs, laboratory reagents, medical and diagnostic equipment are available from the Medical Stores Departments (MSD) [35]. Office furniture, equipment and supplies prices are available from the Tanzania Government Procurement Services Agency [36]. Building space prices are available at the National Housing Corporation (NHC), or the Tanzania Building Agency (TBA). However, some care is needed before price data can be considered acceptable. Prices may not reflect real resource use and their opportunity cost. For example, prices for vaccines and HIV/AIDS drugs in most developing countries may involve subsidies. When considering the societal perspective, it is most appropriate to use full costs.

The cost of capital resources such as medical equipment, buildings and land will appear as a single large amount at the beginning of an evaluation period. The value of these costs could be "shared" over the life of the project, by calculating the equivalent

annual costs, through annualising the initial capital outlay over the useful life of the asset [27, 37]. This can be done as follows:

$$E = \frac{K - (S/(1+r)^n)}{A(n, r)} \quad (1)$$

Where  $E$  is the equivalent annual cost,  $K$  is the purchase price,  $S$  is the resale value,  $r$  is the interest rate and  $n$  is the useful life of the item.  $A(n, r)$  is the annuity factor ( $n$  years at interest  $r$ ), expressed as  $(1 - (1+r)^{-n})/r$ .

### 2.3.4 Unit cost

The costs in each cost centre are added to obtain the total cost. The total cost is then divided by the intervention output to provide the unit cost of delivering the intervention, for example, the cost of outpatient treatment of diarrhoea in children under five or the unit cost of providing a dose of pneumococcal vaccine. The unit cost may be applied in calculating the cost-effectiveness of the study intervention.

## 2.4 Measuring health consequences

The main objective of measuring health consequences in the economic evaluation framework is to determine any change in the health outcomes of relevant curative or preventive health interventions being compared [30]. The outcome measures may be disease specific e.g. the number of diarrhoea episodes prevented by rotavirus vaccination, the number of hospital visits prevented by pneumococcal vaccination among children under five etc.[29]. These measures only enable comparisons between interventions producing the same outcomes. However, with the use of a generic outcome measure e.g. Disability Adjusted Life Years (DALYs) or Quality Adjusted Life Years (QALYs), which incorporates both years of life lost due to premature mortality and morbidity, CEA enables comparison of cost and outcome results between competing interventions within and/or between disease spectrums, for example, DALYs averted or QALYs gained with diarrhoea vaccination or primary prevention of CVD [30].

### 2.4.1 Quality-adjusted life years (QALYs)

Quality-adjusted life years are units of health care outcomes that adjusts gains in years of life subsequent to a health care intervention by the quality of life during those years [38]. It is calculated by multiplying the number of life years gained through treatment by the Health Related Quality of Life Index (HRQoL) for each year. The index is set with 1 equalling perfect health and death given a value of zero. This can be expressed as [39]:

$$QALYs = \sum_{t=a}^{a+L} Q_t \quad (2)$$

Where L is the remaining life expectancy of an individual at age a, t equals life years of the individuals within that life expectancy and Q equals the HRQoL index.

Figure 2 below illustrates health outcomes for two children, A and B. Child B receives a full dose of pneumococcal vaccine, with QALYs gained being the number of life years on the X axis multiplied with the corresponding HRQoL index on the Y axis until death (area B). For child A, who receives no vaccine his QALYs are equivalent to the life years on the X axis until death multiplied with the HRQoL index on the Y axis (area A). Health Benefit (QALYs) due to Pneumococcal vaccine = QALY in area B – QALY in area A.

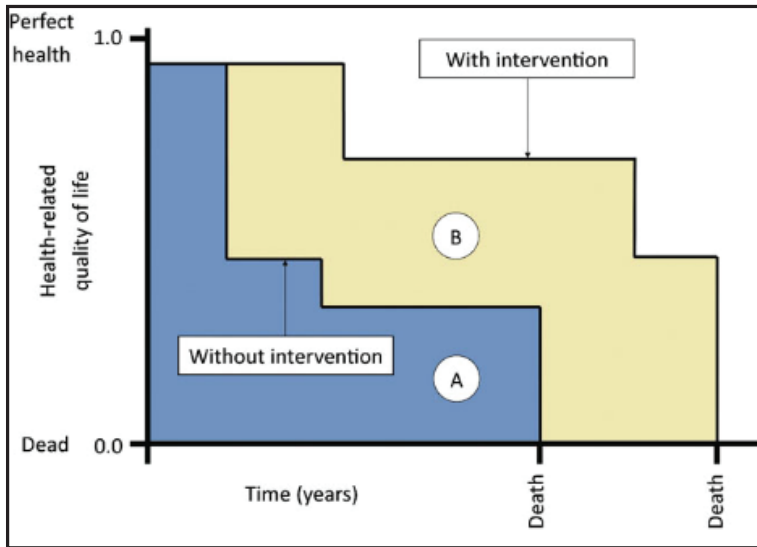


Figure 2: Quality-adjusted life years without intervention (area A) and the resulting QALYs gain associated with the intervention (area B)

#### 2.4.2 Disability Adjusted Life Years (DALYs)

Disability-adjusted life years (DALYs) is a unit that combines mortality and morbidity to express loss in health. It is the sum of premature mortality measured as years of life lost (YLLs) and the period spent in a non-fatal health condition (morbidity) due to disease or injury, measured as years of life lived with disability (YLDs) [40]. The years of life lost (YLLs) due to premature mortality is the difference between age at death and the expected life expectancy either from country specific life tables or the ideal standard life expectancy at each age computed by the Global Burden of Disease (GBD) study [41]. The years of life lived with disability (YLDs) are computed as duration of illness or disability multiplied by the disability weights, the disability weights for about 291 diseases and injuries have been computed by the GBD study [40]. DALYs computation can be summarised as:

$$\text{DALYs} = \text{YLL} + \text{YLD} \quad (3)$$

The disability weights have an index of zero as perfect health and one as worst health. Figure 3 below presents the DALYs of a young woman who is diagnosed with iodine-deficiency goitre at 10 years with a disability weight of 0.2 [40], at age 50 she

passes away with disability weight of 1 (worst health i.e. death), assuming the life expectancy at age 50 is 80 years. The loss in health calculated in DALYs will be equal to  $40 \times 0.2 = 8$  YLDs and  $30 \times 1 = 30$  YLLs. Therefore the DALY loss will be equal to  $8 + 30 = 38$ .

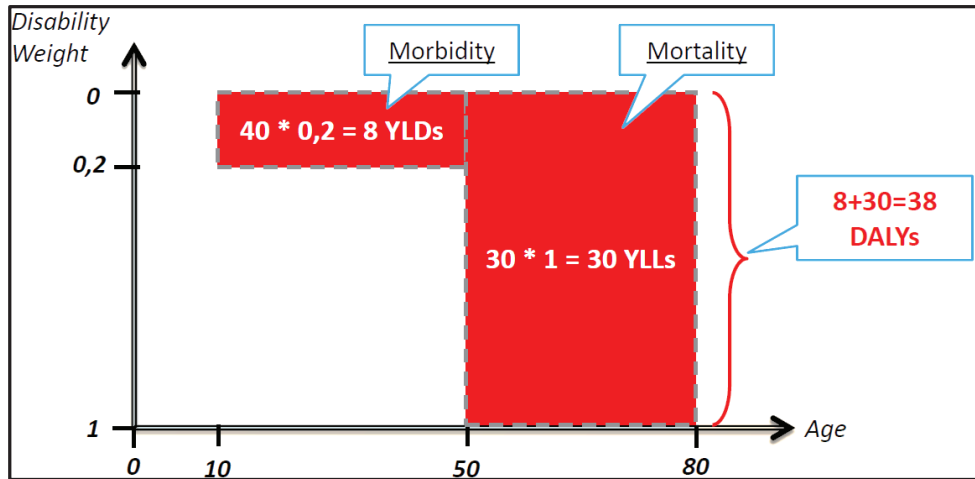


Figure 3: Diagram presenting the loss of health life years in a course of an individual life time

### 2.4.3 Age weighting

In the original GBD study 1990, higher weight to adults of working age and lower weight to young children and the elderly were assigned [42]. The authors of the study argued that children and the elderly are socially and economically dependent on adults of a productive age [43]. However the GBD 2010, in response to moral and equity concerns [44, 45], excluded age weighting in the calculation of disability weights. In this thesis, age weighting has not been included.

### 2.4.4 Health outcome valuation

The values for the HRQoL, or the disability weights, are generated through different methods of eliciting preferences in ranking different diseases and injuries. The study participants may be patients, the general population or health professionals. The methods mainly used are standard gamble, time trade-off, visual analogue scales or person trade-off. In *Standard gamble (SG)* subjects are asked to gamble between a

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good and bad outcome offered with odds and an intermediate outcome offered with certainty. For example which would you prefer the certainty of being in the current state or a 50% chance of being in perfect health or a 50% chance of being dead? In ***Time trade off (TTO)***, subjects are asked to make choices between health states of different duration. For example would you prefer five years in your current state of health or two years in perfect health? Time in different health states is varied until the individual is indifferent to choice. Another method is the ***visual analogue scale (VAS)***. In this, subjects are asked to give some value to a described health state on a visual analogue scale like a thermometer. The worst state is 0 and the best is 100. **Person trade-off (PTO)** is used in eliciting people's preferences. In this method individuals are asked to choose between saving one life or treating a number of people (N) with a certain disease (X) [27-29]. The paired comparison method was used in the 2010 GBD study to estimate the disability weights of the DALYs. Respondents were presented with description of symptoms and the possible functional limitations of two hypothetical diseases and resulting sequelae. The respondents were asked to choose who they would consider healthier of two individuals in different health states [40].

In cost-benefit studies, monetary terms are used to value health outcomes. Methods such as discrete choice experiments and revealed preferences may be used to elicit these values. Another method is the human capital approach where individuals are valued by their productive worth. Hence life years are valued in terms of expected earnings. A third method is the willingness-to-pay approach where individuals are asked how much they would be willing to pay for a given health improvement. The pros and cons of applying the CBA valuation of health outcomes have been documented previously [46, 47]. However the CBA method is not used in this thesis.

## 2.5 Decision modelling

To obtain the cost-effectiveness results, the cost and outcomes for the intervention and for any alternatives under evaluation have to be combined into a single measure. The economic evaluation analysis may be undertaken alongside a randomised

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controlled trial using patient-level data [48]. The trial-based economic evaluation provides limited comparisons as, often, not all possible alternatives are included. Trials may have limited follow-up period. There may be more than one trial providing similar evidence [28]. To account for the bottlenecks encountered in trial-based evaluations, the use of decision analytic modelling has been proposed and widely used [49]. Decision analytic models involve specifying a decision by quantifying alternative health interventions in terms of probabilities and evidence on costs and health benefit to determine the optimal choice for decision making. These probabilities involve determining the likelihood that individuals will have one pathway or state rather than another, that is, being alive, recovering with non-fatal outcomes or dying after an intervention. The modelling techniques applied in economic evaluation of health intervention include decision trees, Markov models, micro simulation or patient-level simulation, discrete event simulations and dynamic models [49]. For the purpose of this thesis, we will use the decision tree and Markov modelling techniques.

### 2.5.1 Decision tree

A decision tree (Figure 4) is represented by a sequence of branches, each representing an alternative event that may occur in the interventions under evaluation [28, 49]. The square green box represents the decision node where a decision question is presented. The blue circular nodes are chance nodes, presenting the probability of an event's occurring e.g. of the new treatment's being a success or a failure. The probability of each event's occurring on the chance node is mutually exclusive and often adds up to 1. The triangular red box is the terminal node, where the payoff values are assigned. This may include cost, utility etc. depending on the study objective.

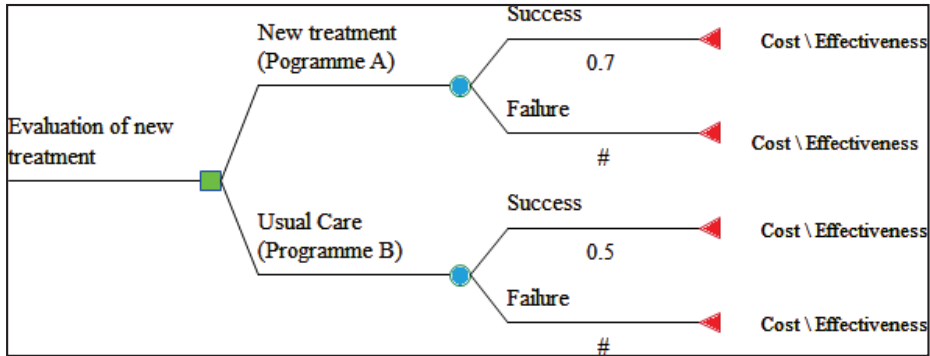


Figure 4: A simple decision tree presenting the decision question and the alternative interventions

Building decision trees, especially for chronic or infectious diseases with recurrence, may require many pathways making them very complicated or “bushy”. An alternative type of model is a Markov model.

### 2.5.2 Markov model

Markov models allow a research question to be set in such a way that continuity and repetition of events are allowed. The patient is allowed to move between the health states in defined time intervals, commonly known as cycles [28, 49].

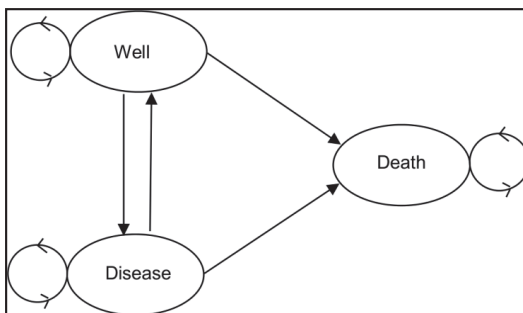


Figure 5: A Markov transition model presenting three disease states with recurrent events

The policy question under evaluation determines the quantity of health states and the length of a cycle. The health states are mutually exclusive, ie, the patient can only be in one state at a time. In this model (Figure 5), it is assumed the patient in each period can stay well, have a disease or die. Similarly a patient could recover and become



well, have a relapse and catch a disease or die. The sum of the probability in each cycle must be equal to one. At the end of each cycle, costs and outcome values weighed by the cohort remaining in the cycle are accrued to reflect the reward of being in that cycle. Total rewards are determined at the end of the Markov process by totalling all the cycle rewards. In some cases, they may be “one time” rewards which should be included. The termination of the Markov model is governed by pre-defined rules. It could be that the model runs until all members are dead i.e. the absorbing state or at a stated cycle.

## 2.6 Presenting and interpreting cost-effectiveness results

Presenting results of cost-effectiveness analysis can be challenging. An example can illustrate the ideal. If there are two programmes (1) and (2) with expected costs of US\$ 2000 and US\$ 1000 and expected DALYs averted of 0.4 and 0.5 respectively, which programme should be selected? Using “average” cost-effectiveness indicates that programme 2 is the optimal choice, as it has the lowest cost per health outcome. However, the famous sixth stool guaiac study [50], indicates that the “incremental”, that is the additional cost and effects, matter in presenting the cost-effectiveness results. The incremental cost-effectiveness ratio (ICER) provides additional information on the incremental cost generated by one intervention over another compared to the additional effects [27]. This can be articulated as;

$$\text{ICER} = \frac{C_1 - C_2}{E_1 - E_2} \quad \text{or} \quad \frac{\Delta C}{\Delta E} \quad (5)$$

Where  $C_1$  and  $E_1$  are costs and effectiveness of the new intervention, and  $C_2$  and  $E_2$  are the cost and effectiveness of the alternatives being compared respectively.

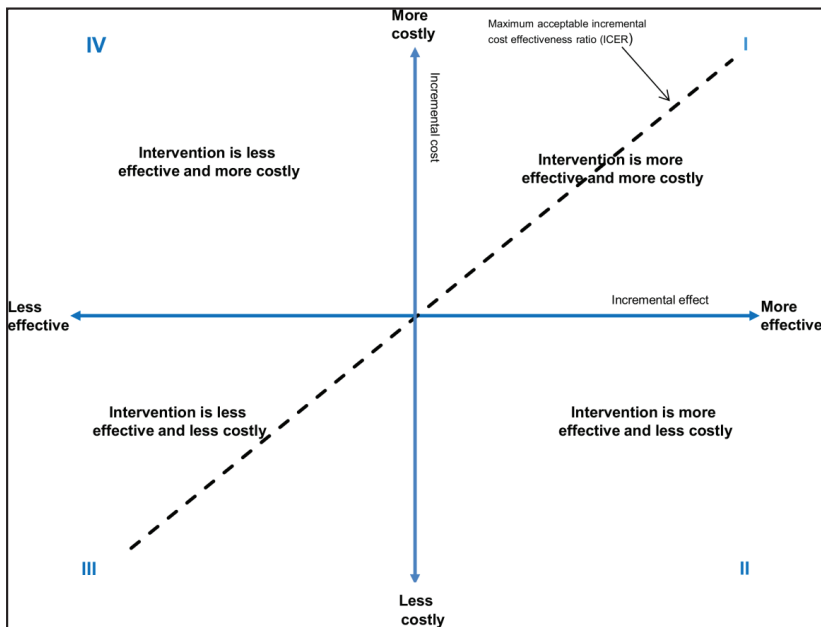
Cost-effectiveness analysis may provide a range of potential outcomes and often it is not possible to draw a straightforward conclusion (Table 3).

**Table 4: Comparison of incremental effectiveness and costs of new intervention (A) compared to usual care (B)**

		Cost		
		A<B	A=B	B<A
Effectiveness	A>B	(A) Dominant	(A) preferred	Unclear
	A=B	(A) preferred	Both equivalent	(B) preferred
	B>A	Unclear	(B) preferred	(B) Dominant

Source[27]

From Table 4, if new intervention (A) uses few resources and yields more health benefit compared to the usual care programme (B), the new intervention (A) is dominant. Where the new intervention programme (A) provides more benefit but costs more, the decision remains unclear. This can be represented on a cost-effectiveness plane for more clarity [51].



Source [27]

**Figure 6: The cost-effectiveness plane. The x axis displays the incremental effectiveness between the new intervention and the comparator and the y axis shows incremental cost. The slope of the line from any point on the figure to the point of intersection is the incremental cost-effectiveness ratio.**

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The y-axis in figure 6 above, presents the incremental cost and the x-axis presents the incremental effectiveness of the new intervention versus the comparator. The new intervention on a second quadrant dominates, i.e. provides more benefits at a lesser cost hence poses no challenge to a policy decision to adopt the new intervention. In the fourth quadrant, the new intervention provides less benefit at larger cost compared to the usual care. The new intervention in this case will be dominated. A decision to reject the new intervention will therefore be straightforward. In quadrants I and III the decision about the introduction of a new intervention is not clear. In quadrant I the new intervention offers more benefits at higher cost, while in quadrant III the new intervention costs less but provides less benefit than the comparator. To determine whether or not to accept the new intervention, a trade-off has to be made, either to choose greater benefits at a higher cost or smaller benefit for a lower cost.

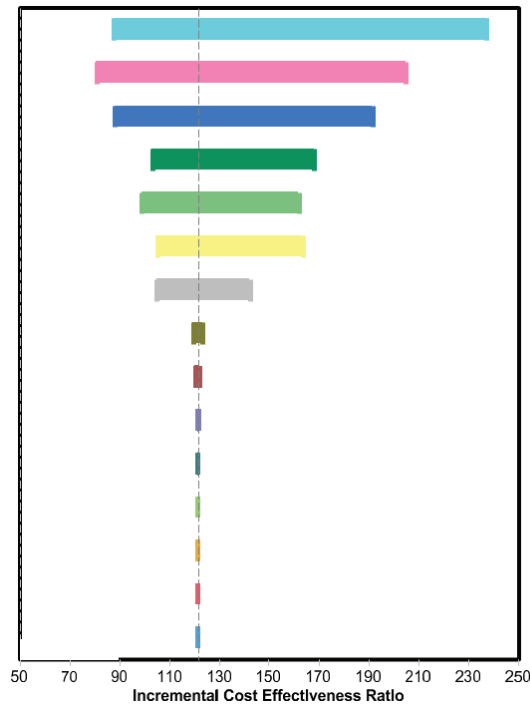
To reach an informed decision about adopting or rejecting the new intervention in the situations in quadrant I & III, a standard approach is to have a threshold value for health benefit i.e. a maximum willingness to pay (WTP) for health (depicted by the dotted line running through the CE plane (Figure 4)). Using this threshold value for the DALY averted or QALY gained, it would be possible to recommend the adoption of a new intervention that yielded an incremental cost-effectiveness ratio (ICER) below the stated threshold [27, 28]. Making a decision to accept or reject a new intervention based on point estimate ICERs may not provide adequate information for maximising resource allocation by policy makers. Uncertainty and sensitivity analysis surrounding the ICERs provides additional useful information.

## 2.7 Uncertainty and Sensitivity Analysis

### 2.7.1 Deterministic sensitivity analysis

In this type of sensitivity analysis individual parameters are varied using point estimates (e.g. lowest and highest value) to determine the influence of each parameter on the incremental cost-effectiveness results [27, 28]. The results of deterministic

sensitivity analysis can be visually presented e.g. using the tornado diagram (Figure 7).



Source [52]

**Figure 7: A tornado diagram representing one-way sensitivity analysis results.**

The horizontal bars illustrate the one-way sensitivity analysis outcomes. The vertical dotted line represents the baseline ICER result. The influence of each input parameter on the model outcome can be evaluated relative to the baseline results [52].

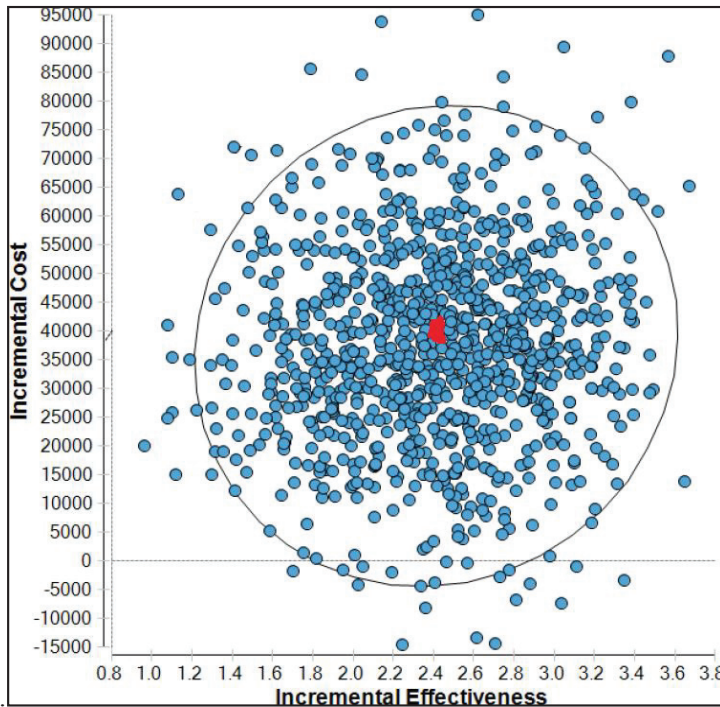
### 2.7.2 Probabilistic sensitivity analysis

The uncertainty surrounding the ICER results is contributed by different estimates in the model. Therefore interaction of all model parameters simultaneously is essential to estimate correctly the uncertainty in the model parameters [53, 54]. The probabilistic sensitivity analysis (PSA) uses the distribution around the mean to estimate the uncertainty surrounding the values of the model inputs [27]. The choice of the type of distribution depends on the evidence available on the particular input

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parameter [28]. There are some recommendations on the nature of the distribution for different model input parameters. For probabilities, the beta distribution is recommended, since this constrains probabilities to lie between zero and one. Gamma distribution is recommended for costs, since this prevents negative cost value and allows for the fact that costs are usually positively skewed. Log-normal distribution is recommended for ratios such as effectiveness values. For utilities, the beta distribution is preferred, assuming that utility values are above zero [54, 55]. Simultaneously and repeatedly the distributions of all parameters are drawn randomly. The process of repeated random sampling is known as Monte Carlo simulation. The model is run for each combination of parameter estimate a large number of times (e.g. 1000 times) generating pairs of cost and effects. The resulting pairs are then used to estimate a 95% confidence range of the incremental costs and effects [27, 28].

The pairs of incremental cost and effects from the Monte Carlo simulations can be plotted on the cost-effectiveness plane using a scatter plot graph (Figure 8). The red circle in figure 8 indicates the base-case results. The circular blue dots indicate the uncertainty surrounding the base-case incremental cost and effects. The spread of the blue dots on the y-axis indicates the uncertainty in incremental cost (US\$ -15000 to US\$ 95,000). On the x-axis the density of the blue dots indicates the uncertainty in incremental effectiveness (1 to 3.8 DALYs). The joint density of incremental cost and effects in the scatter plot depicts the uncertainty around the ICER result. To provide decision makers with clearer illustration to aid decisions on accepting or rejecting a new intervention given the willingness to pay for health, the cost-effectiveness acceptability curve may also be used [53, 54].



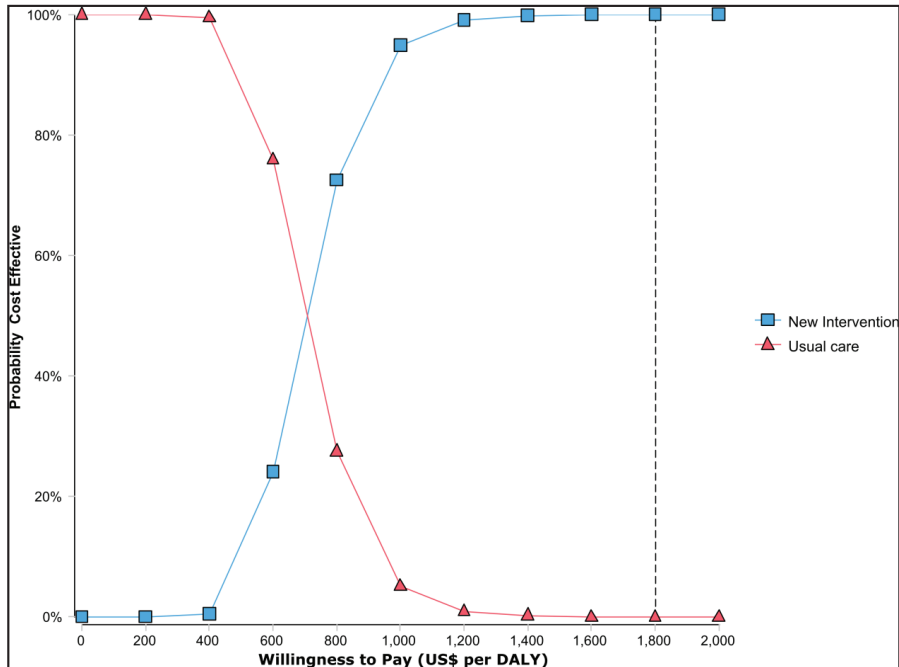
Source [56]

**Figure 8: A scatter plot of incremental cost (US\$) vs incremental effectiveness (DALYs) (e.g. intervention (A) vs usual care (B)).**

### 2.7.3 Cost-effectiveness acceptability curves

The uncertainty surrounding the probability that the new intervention will be cost-effective compared to existing care may be illustrated using the cost-effectiveness acceptability curve. The pairs of incremental cost and effects from the Monte Carlo simulations are used to plot a curve (Figure 9). The probability that a cost-effect pair falls within the WTP threshold is plotted on the y-axis (vertical axis). The willingness to pay for health (WTP) is plotted on the x-axis (horizontal axis). The black dotted line indicates a ceiling WTP, in this case equivalent to three times Tanzania 2012 GDP per capita value of US\$ 609 [57]. This benchmark of a WTP value of three times the GDP is one proposed by WHO for low income countries [58]. In the example provided in figure 9 below, the new intervention has a 100% probability of being cost-effective far below the proposed willingness to pay for health for Tanzania

compared to usual care. The cost-effectiveness acceptability curve provides potential information to decision makers on the optimal allocation of scarce resources within a finite health care budget.



Source (Authors)

**Figure 9: Cost-effectiveness acceptability curve**

## 2.8 Discounting costs and effectiveness

Costs and consequences often occur at different times. People value benefits higher in the present than in the future, and seek to delay paying costs; the postponement is motivated by the notion that resources not spent immediately, may allow for investment with a return in real time [27, 37]. Similarly in health care, individuals often have preferences in favour of immediate rather than hypothetical future health outcomes, therefore it may be appropriate to discount future health to some extent that reflects people's preferences. However, there has been critique of discounting health outcomes. Opponents argue that there is no moral or ethical justification for applying the economic theories in discounting health benefits [59]. There is no

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agreement on the handling of such controversial issues in discounting health benefit or the discount rate to be applied. The most common practice in economic evaluation is to apply a similar discount rate for cost and health benefit. WHO-CHOICE(Choosing Interventions that are Cost-Effective) recommends a discount rate of 3% for cost and health benefit in developing countries [30]. Sensitivity analysis employing a discount rate of 0%, and 6% is also recommended. Obtaining present values can be done using the formula below [37].

$$PV = \frac{K}{(1+r)^t} \quad (4)$$

Where  $PV$  is the present value,  $K$  is costs or consequences,  $t$  is the period in which the costs or consequence occur and  $r$  is the discount rate.

## 2.9 Limitations of economic evaluation

Economic evaluation is principally concerned with allocative efficiency, that is, are scarce resources being used to produce the maximum amount of health possible? However, efficient solutions may not always be fair and some groups may benefit more than others [60, 61]. To address distributional concerns in economic evaluation it is proposed that some efficiency is traded for equity [61, 62]. Methods of incorporating equity concerns into economic evaluation are not well developed, but some have been proposed [63-65], see Johri and Norheim, 2012 [66]. However, it is imperative that cost-effectiveness and equity analysis results are interpreted critically in line with available ethical principles for resource allocation [59].



### **3.0 Equity in health and health care**

Equity in health refers to the absence of avoidable unequal and unfair differences in health and health outcomes in the population [67-69], for example, uneven distribution of health determined by income levels or differences due to geographical location within groups of population. Concerns for equity in health care entail achieving equal access, use and quality of available health care for people with the same levels of need [67]. There are two terms commonly applied in the literature regarding equity; inequality and inequity. In some literature the terms have been used interchangeably. However for the purpose of this thesis inequality denotes the variations in health within the population and inequity refers to differences in health that are judged as unfair. Not all inequalities are unfair. One example is the natural difference in life expectancy between male and females. Females have higher life expectancy than males, and if these are biologically determined, they may not be seen as unfair [70]. The degree of inequality can be used as a mark of inequity [71]. The concept of health equity is multifaceted with moral and ethical dimensions [67]. To make a judgement whether the health inequality in a particular society signifies inequity in health requires empirical and normative analysis of the underlying cause within that society [72].

Inequities in health are well documented. Access and use of health care is likely to favour the affluent population who may have less need for the services compared to poorer counterparts [73]. Inequity in health occurs not only in affluent urban areas, but also in presumed uniformly poor remote rural areas, where relatively rich families are more likely than poorer families to seek and obtain medical care [74]. However, health care is not the only determinant of health [75]. Other factors are associated with inequalities in health, such as income or wealth, education, occupation, ethnicity, gender, residential area (urban/rural), or immigrant status [76]. Health care alone cannot lead to an equal distribution of health; a focus on social determinants of health is therefore another important element in addressing health inequity.

Health inequities are consequences of unfair distributions of economic resources, political and social authority between groups in society [68]. It is imperative that available methods to examine socioeconomic disparities in health states and service delivery are used critically to examine population access to health programmes and other social determinants of health [77]. Household data sets, from the Demographic and Health Survey (DHS) are important sources for the measurement of a variety of aspects of health inequality [78]. Critical examination of equity trends from available data in Tanzania can inform the national health policy agenda.

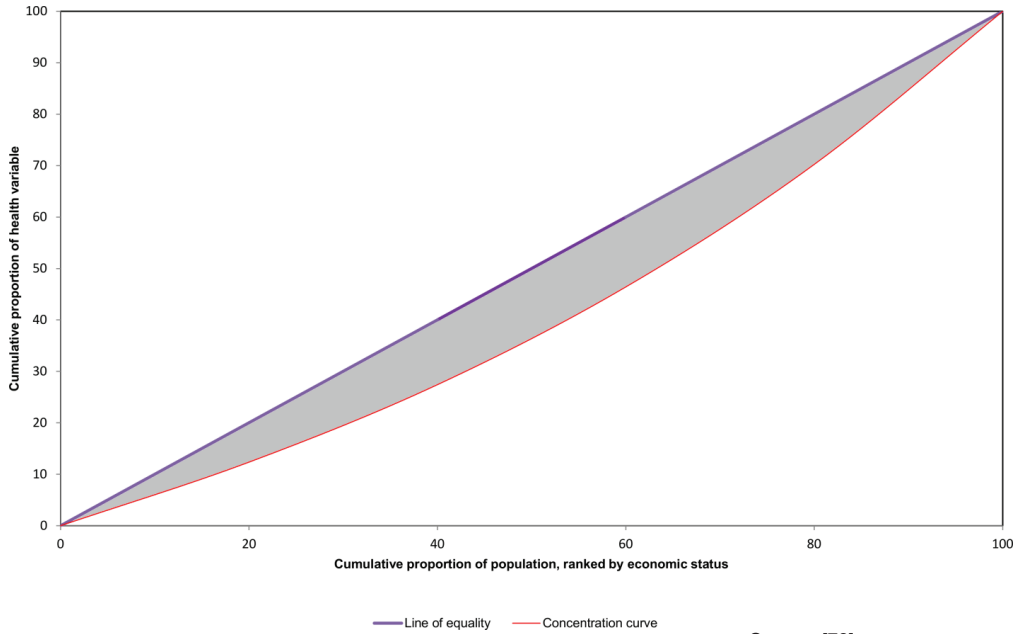
### 3.1 Measuring inequalities in health and health care.

The concentration curve and concentration index are the most commonly applied methods of quantifying inequality in health outcome or any other health variables such as intervention coverage or vaccination status.

#### 3.1.1 Concentration curve

Group of individuals are ranked from low socioeconomic status to higher using a measure of life standard such as income levels of the socioeconomic quintile. The cumulative proportion of the population group categorized by socioeconomic wealth index is then plotted against the cumulative proportion of the health variable of interest. The cumulative population ranking is plotted on the x-axis and the cumulative health variable on the y-axis [78].

The concentration curves depict the degree of socioeconomic inequity related to the distribution of a health variable between different population groups. When the concentration curve coincides with the line of equality, this indicates that there is no socioeconomic inequality. If the curve is below the line of equality, this indicates that the health variable is concentrated in the richest population, and if above the line it indicates that the health variable is concentrated in the poorest population. The further the concentration curve lies from the line of equality the larger the inequality. From figure 10, the concentration curve lies below the line of equality, indicating that the variable of interest is concentrated in the richest population.



Source: [78]

**Figure 10: Concentration curves of the health variable in a population ranked by socioeconomic status**

### 3.1.2 Concentration index

The concentration index (CI) can be defined as twice the area between the concentration curve and the line of equality (marked by grey colour, figure 10 above) [78]. The index measures the degree of socioeconomic inequality. Using grouped data, given a number of groups  $T$  the concentration index (CI), can be computed using a spreadsheet [78], by applying the following formula below or using most statistical software such as stata.

$$CI = (p_1 + l_1) + (p_2 + l_2) + (p_3 + l_3) + \dots + (p_{T-1}L_T - p_T L_{T-1}) \quad (5)$$

Where  $p$  is the cumulative percentage of the sample ranked by economic status, and  $L$  represents the concentration curve ordinate of the corresponding groups.

The value of the concentration index lies between -1 and +1, with a zero value indicating absence of socioeconomic inequality. The concentration index is closely related to the concentration curve (Figure 10 above). When the concentration curve lies above the line of equality, the concentration index takes a negative value, indicating that the distribution of the health variable favours the poor. When the curve lies below the line of equality the index takes a positive value indicating the health variable of interest is concentrated among the richest. In the case of undesirable health variables such as mortality or morbidity, a negative value of the concentration index indicates that mortality is concentrated among the poor.

The information generated can be critically evaluated using moral and ethical principles to ascertain if the observed inequalities are inequities. The consensus reached by either a national priority setting committee; researchers, academicians or decision makers could aid decision makers in fair resource allocation and integrate equity concerns into national health policy and strategies.

## 4.0 Priority setting in health care

### 4.1 Evidence for priority setting

Health care priority setting is a complex undertaking. The process involves making critical decisions on health care delivery, including what interventions to fund within limited national health care budgets, and their distributional impact. The undertaking draws information from many sources and different disciplines; such as burden of disease in the population, cost-effectiveness and equity analysis [79]. New discoveries of treatment and health care technologies have increased the need for priority setting. The discoveries increase options for diagnosis and management of diseases but also increase costs, hence the need for informed decisions in allocating limited resources. Caution is needed when making decisions to fund new, effective but costly interventions, when cheaper, slightly less effective options are available, since choosing the newer option could actually lead to less health improvement in the population. In such contexts, it is important that evidence informs priority setting in order to ensure wise use of limited resources [80].

The burden of disease evidence could be used to set the agenda in the priority setting process. Table 5 presents the rank order of the twenty five diseases with the highest burden in Tanzania [81]. This information can be used to establish the main domain of interest. Further empirical research may be conducted to determine the cost-effectiveness of interventions which address these major disease conditions. The combined evidence from CEA and equity impact analysis can be used to inform and revise the Tanzania National essential health package and monitor implementation. However, during this process, neglected diseases may need special care, since they often affect smaller patient groups, and are therefore likely to have a lower disease burden. If only the burden of disease information is used to set the agenda, already neglected diseases may become further neglected. This may require a separate analysis and priority setting process for neglected disease (see also Table 2).

**Table 5: Burden of disease in Tanzania ranked by percentage proportion of Disability Adjusted Life Years (DALY) from 1990 to 2010**

Rank	Disorder	% proportion of total DALYs
1	HIV/AIDS	17.3 %
2	Malaria	11.8 %
3	Lower respiratory infections	7.5 %
4	Diarrhoeal diseases	3.8 %
5	Neonatal encephalopathy	3.4 %
6	Preterm birth complications	3.1 %
7	Protein-energy malnutrition	2.6 %
8	Iron deficiency anaemia	2.4 %
9	Neonatal sepsis	2.4 %
10	Syphilis	2.3 %
11	Road injury	2.1 %
12	Tuberculosis	1.9 %
13	Maternal disorders	2.0 %
14	Major depressive disorder	1.8 %
15	Epilepsy	1.2 %
16	Low back pain	1.3 %
17	Congenital anomalies	1.0 %
18	Meningitis	0.9 %
19	Fire	0.9 %
20	Chronic obstructive pulmonary disease	0.9 %
21	Interpersonal violence	0.8 %
22	Drowning	0.8 %
23	Stroke	0.8 %
24	Ischemic heart disease	0.7 %
25	Anxiety disorder	0.8 %

Source: [81]

## 4.2 Priority setting framework

Decisions on health care resource allocation in Tanzania are guided by the essential health package (Table 2), developed almost two decades ago [10]. This has been updated from time to time [24], however, with limited use of evidence. New techniques to aid priority setting procedures have been developed [82]. The cost-effectiveness evidence base has been broadened using empirical studies and global health projects, such as the WHO-CHOICE and the Disease Control Priorities projects [30, 83-85]. Policy modelling tools, providing evidence to support priority setting, such as the Lives Saved Tool (LiST) developed by the Futures Institute of the

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Johns Hopkins University have evolved [86]. Data on the burden of disease are continuously being updated [87]. Recently, there have been initiatives to compose new guidelines to assist country-specific priority-setting procedures. Such documents include guidelines on incorporating equity concerns alongside cost-effectiveness in setting health care priorities that ensure universal coverage [26, 88]. These documents recommend inclusion of cost-effective interventions that address diseases with the highest burden, particularly those affecting the worst-off population, and ensure financial risk protection.

To identify the best combination of health interventions addressing the major burden of disease, while maximising health benefit and targeting the worst off population, one needs a framework which integrates information on cost-effectiveness, equity impact and available resources. Cost-effectiveness results may be used as a foundation for the priority setting framework [76]. The WHO proposes ranking interventions into three categories based on willingness to Pay (WTP) threshold equivalent to one to three times the gross national per capita income (GDP). Interventions produced at a cost of less than the average annual national GDP may be categorised as highly cost-effective, those costing above the annual GDP but less than three times the GDP can be classified as cost-effective and those costing above three times GDP would be considered as not cost-effective [58].

A WHO report on making fair choices towards universal health coverage [89]; proposes that interventions are classified into three categories according to priorities, high, medium and low priority. The classification is based on three main criteria: cost-effectiveness of the intervention; the extent to which the intervention addresses the health needs of the worst-off population; and financial risk protection against catastrophic health expenditures among the population. If we apply the WHO recommendations in a priority-setting framework the interventions may be ranked thus: the interventions that are both highly cost-effective and address the health needs of the worst off population should be classified as high priority. Subsequently interventions that are cost-effective and address the health needs of the vulnerable population may be classified as medium priority. Interventions that are less cost-

effective and where there is not enough evidence on the benefits for the worse-off populations may be classified as low priority. The degree of financial risk protection may be used to further adjust the ranking.

The proposed classification aims to help the decision-making process. Decision makers should justify their choice if cost-effective (medium priority) or less cost-effective (low priority) interventions are implemented before highly cost-effective interventions [89, 90]. Essential health packages developed according to these criteria may ensure more fairness and equitable access while countries are moving towards universal coverage.

### **Willingness to pay threshold (WTP)**

The use of the WHO standard willingness-to-pay threshold (WTP) has recently created a lot of discussion [91-93]. It has been argued that the threshold lacks a foundation of empirical evidence [92, 93], and that it has limited application in developing countries [91]. The use of the WHO WTP threshold may be overly optimistic. A study in United Kingdom (UK) reveals that the empirical threshold of health forgone through resources being committed to particular interventions was only 52% of the per capita GDP in that country [94]. Since the GDP of lower income countries is far less than that of UK, and the resources committed for the health system in this countries is far lower than those reported in UK, the benchmark in low income countries may not be higher than 52 % of GDP [93, 94] . Health care priority setting works within a finite budget. Implementing all interventions, which cost less than three times the GDP in Tanzania, may replace services with higher value. The available health care budget should dictate the threshold and mix of cost-effective interventions to be included in the minimum essential health package [91]. The threshold for cost-effectiveness for health should be based on the country's ability to finance cost-effective interventions, and will most likely be less than three times the GDP.



## 5.0 Research gap

Efforts have been made to expand interventions combating mortality and morbidity in mothers and children under five in Tanzania. Strategic plans and policies for the reduction of maternal and child deaths have been formulated. However, there is still a need for more evidence to inform maternal and child health priority setting. Investment in interventions to reduce maternal and under-five morbidity and mortality requires a focused approach, guided by scientific evidence and normative equity analysis. Validated tools to assist the integration of burden of disease evidence, effectiveness, equity and costs of intervention scale up are now available. These tools are seldom used in Tanzania, so decisions about resource allocation often depend on professional opinions and consensus, which is often inefficient and inequitable as, for example, in the selection of essential drugs [95].

There is a need for country-specific evidence in several areas of maternal and child health. This evidence needs to be relevant for policy makers, health planners and other stakeholders so it can turn poor performance and under-investment into fair and efficient resource allocation, and ultimately lead to better services, more lives saved and improved maternal and child health.

## **6.0 Study objectives**

### **6.1 General Objective**

The aim of the study is to generate evidence on a selection of maternal and child health interventions so this can inform priority-setting decisions in the direction of increased coverage for effective interventions that improve health outcomes and redress inequity.

### **6.2 Specific Objectives**

1. To estimate cost and cost-effectiveness of rolling out rotavirus vaccine compared to existing treatment strategies against diarrhoea among children in Tanzania.
2. To estimate cost and cost-effectiveness of introducing the 13-valent pneumococcal conjugate vaccine (PCV13) compared to the 10-valent pneumococcal (PCV10) and compared to no vaccination in Tanzania.
3. To estimate the potential health gains and equity impact if coverage of a set of high impact priority maternal and child health interventions were scaled up to the national universal coverage targets for achieving MDGs in Tanzania.

## 7.0 Materials and methods

### 7.1 Selection of study interventions

The burden of disease information from the global burden of disease study specific for Tanzania [81], was used to select disease conditions with the highest burden to be included in the study. For the purpose of our study and in reference to burden of disease in Tanzania (table 4), we included key interventions addressing maternal and child health. In papers I and II, we included interventions on pneumonia and diarrhoea for cost-effectiveness analysis. In paper III, we included a mix of multiple interventions on malaria, pneumonia, diarrhoea and maternal conditions for the analysis of equity and health impact of scaling up the interventions. Further details on interventions are provided in section 7.4.1 below.

### 7.2 Data sources

The two economic evaluation studies employed both primary and secondary data. Primary data were collected from two regions, Dar es Salaam and Pwani in Tanzania. From each region, one district was randomly selected: Ilala in Dar es Salaam region and Kisarawe in Pwani region. The selected study areas represent health care delivery in urban (Dar es Salaam) and rural areas (Pwani). Data on costs and coverage for selected maternal and under-five interventions were obtained from one district hospital and a health centre in each district. Secondary data on national level intervention coverage, effectiveness and epidemiological data were retrieved from published literature and government reports.

### 7.3 Costs data

Costs data used in **Papers I and II** were collected from two districts in 2012, for the one year period July 2011 to June 2012. In each district, data were collected from one hospital - Amana Hospital for Ilala and Kisarawe Hospital for Kisarawe district - and one health centre, Chanika for Ilala and Masaki for Kisarawe. The ingredient

approach was used to identify, measure and value the cost of rolling out rotavirus and pneumococcal vaccine and the costs involved in treating moderate (outpatient) and severe (inpatient) diarrhoea and pneumonia cases. A detailed explanation of the costing method is provided in chapter 2.3.

### 7.3.1 **Cost data collection**

The resources available in each health facility were classified into two main categories, recurrent and capital goods. Capital items included buildings, medical equipment such as oxygen concentrator; drip stands, etc. and non-medical equipment such as vehicles, vaccine storage rooms, refrigerators, patient beds, chairs, and tables. Recurrent resources included personnel; drugs; medical supply e.g. syringes cannulas, infusion sets, etc.; non-medical supplies e.g. linen, papers, pens, cleaning materials etc. Recurrent costs also included electricity and water bills, general building maintenance, vehicle fuel and maintenance. Capital items were physically enumerated and the actual amount of recurrent items used was obtained by reviewing all anonymous health facility records e.g. pharmacy and general store records.

The value of medical equipment and supplies was obtained from the Tanzania drug stores department catalogue [35], and the non-medical supplies and equipment costs were obtained from the Government Procurement Services Agency (GPSA) [36]. The value of building spaces used for immunisation, diarrhoea, and pneumonia treatment was estimated using the state-owned largest housing estate company in Tanzania, the National Housing Corporation. The Bank of Tanzania exchange rates of 2012 were used to translate cost data collected in Tanzania shillings (TSH) to United States dollar (US\$) [96].

### 7.3.2 **Cost data analysis**

The step-down costing method was used to allocate shared costs. Capital costs were annuitized using the Tanzania Central Bank interbank interest rates, the useful life years of capital items were used from the WHO-CHOICE project data. Excel sheets were used for data input and analysis.

### 7.3.3 Presentation of cost data

Cost data are presented as unit costs for diarrhoea management. The unit cost per OPD visit was obtained by dividing total OPD cost (capital and recurrent cost) by the annual OPD under five diarrhoea visits. Inpatient unit costs were obtained by dividing total IPD cost by the total number of IPD bed days used by children suffering from severe diarrhoea and pneumonia. The costs of rolling out rotavirus and pneumococcal vaccines were estimated by dividing the total cost of providing the vaccine by the number of children vaccinated.

### 7.3.4 Ethical considerations

We obtained ethical approval from the ethics committees of the Tanzanian Medical Research Coordinating Committee. The project mainly used anonymous primary cost data and secondary data. We therefore considered that it was not eligible for Regional Ethics Committee approval from Norway, according to the Act on Medical and Health Research, section 4a.

## 7.4 Cost effectiveness and modelling

Cost-effectiveness methods are discussed in chapter two of this thesis; the approaches are used in Papers I and II.

### 7.4.1 Study interventions

#### *Paper I*

This paper evaluates four interventions for the management of diarrhoea: i) the current standard diarrhoea treatment guided by the Integrated Management of Childhood Illness protocol (IMCI); ii) providing only rotavirus vaccine; iii) combining rotavirus vaccination with diarrhoea treatment; and iv) the “do nothing” alternative. The last alternative was considered to reflect a setting without coverage of diarrhoea management interventions.

### *Paper II*

The outcomes of three possible interventions were evaluated: the introduction of pneumococcal vaccines PCV13 or PCV10, and the no intervention scenario, representing settings without coverage of the pneumococcal vaccines.

### *Paper III*

We modelled interventions for prevention and treatment of four key maternal and child health problems. These included interventions targeting safe pregnancy and child birth (antenatal care, facility-based delivery and skilled birth attendant), interventions for diarrhoea management (ORS), pneumonia case management with antibiotic, malaria treatment (Artemisinin combination therapy) and prevention (Insecticide Treated Nets (ITN)).

#### **7.4.2 Epidemiological and effectiveness data**

We conducted a systematic literature search of published and unpublished materials for data on disease epidemiology, intervention effectiveness and coverage rates.

#### **7.4.3 The analytical model**

The modelling techniques in economic evaluation have been elaborated in chapter 2.5 of this thesis.

### *Paper I*

A Markov model was developed using Tree Age Pro (2013). The model runs weekly cycles terminating after 259 weeks (5 years). The child can be in any of the four possible states at a time, ie: well, a health state with no diarrhoea infection, or only with asymptomatic infection; the moderate diarrhoea state; the severe diarrhoea state; and the dead state (it could be death due to diarrhoea or all-cause mortality).

### *Paper II*

A Microsoft Excel based Markov model was employed to run monthly cycles over the cohort lifespan estimated to be 100 years. In each cycle the individual may be in any of the five possible health states related to pneumococcal diseases: the individual

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may have no pneumococcal disease; suffer from all cause pneumonia; or pneumococcal meningitis; or acute otitis media; or pneumococcal bacteraemia; or die from pneumococcal disease or all-cause mortality.

### *Paper III*

Lives Saved Tool (LiST) is a free downloadable software part of the spectrum policy modeling system developed by the Futures Institute of the John Hopkins University [97]. LiST was employed to model the possible health outcomes and equity impact of expanding the coverage of key maternal and child health interventions to the Tanzanian targets set to achieve the MDG within a five year period. Concentration curve and concentration index were employed to measure the equity impact of increased coverage levels to different populations ranked by wealth.

#### **7.4.4 Health outcomes**

Chapter 2.4 of this thesis provides detailed description of measuring health outcomes.

### *Paper I*

Disability adjusted life years (DALYs) were used to estimate the model health outcome. The years lived with disability (YLD) and years of life lost (YLL) in each cycle were accumulated to provide DALYs averted at the termination stage.

### *Paper II*

Health outcomes were measured in QALYs. In each cycle the model totals the gains in QALYs measured as mortality reductions and improved quality of life due to the different interventions.

### *Paper III*

The study reports the health outcome as the number of lives saved (or deaths averted) by expanding the coverage of maternal and child health intervention. The change in the level of inequality is depicted by the concentration curves, and quantitatively, as the change in concentration index before and after increasing the intervention coverage.

#### 7.4.5 Cost effectiveness analysis

The base-case incremental cost-effectiveness ratios (ICERs) for **paper I** were calculated from expected values from the distributions, by dividing the incremental cost of adding a rotavirus vaccine, or diarrhoea treatment interventions or a package of rotavirus vaccine delivered alongside diarrhoea treatment by incremental DALYs averted. We assumed the starting point to be no intervention.

For **paper II**, the base-case ICERs were calculated by dividing the expected distributions of the incremental cost of introducing PCV10 or PCV13 to the incremental QALYs or Life Years saved. The baseline was assumed to be no vaccination. Chapter 2.6 of this thesis provides a description of computing and of presenting cost-effectiveness outcomes.

#### 7.4.6 Sensitivity analyses

One-way sensitivity analysis was performed in **papers I and II** to estimate the influence of individual input parameters on costs and outcomes. The lower and upper bounds of the model inputs were used as model inputs. Probabilistic sensitivity analysis was employed in **papers I and II** to assess robustness of the model outcomes by running multiple model parameters simultaneously. Monte Carlo simulation was used to draw random samples from distributions of input parameters to estimate the probability that interventions were cost-effective relative to the willingness to pay. A detailed description of the methods of analysing and presenting uncertainty in cost-effectiveness is provided in chapter 2.7 of this thesis.



## 8.0 Results

### 8.1 Paper I

#### 8.1.1 Cost

The average total urban/rural weighted cost of rolling out rotavirus vaccine to the current coverage level of DPT-HB vaccine in Tanzania (93%) is estimated to be US\$ 8.4 per vaccine dose. Procuring and distribution of vaccines are the main cost drivers, accounting for 60% and 39% of the total cost in urban and rural areas respectively (Table 2, Paper I).

The cost of a single visit for moderate diarrhoea is US\$ 2.9, and US\$ 4.2 in rural and urban areas respectively. The urban/rural weighted cost per single visit for moderate diarrhoea treatment is US\$ 3.8. The weighted unit cost per bed day for severe diarrhoea is US\$ 8.9 (Table 3, Paper I).

#### 8.1.2 Cost effectiveness

Table 5 (paper I), presents summary baseline cost-effectiveness results. Providing rotavirus vaccine alongside IMCI diarrhoea management at a cost of US\$ 112 per DALY is highly cost-effective at willingness-to-pay threshold equivalent to the 2012 per capita Tanzania gross domestic product (GDP) US\$ 609, compared to providing either diarrhoea management or vaccine alone or no vaccine.

### 8.2 Paper II

#### 8.2.1 Cost

To provide a single pneumococcal vaccine dose costs on average US\$ 7.1 in urban areas and US\$ 11.9 in rural areas at the average national coverage levels of pentavalent vaccine of 93%. The urban/rural weighted unit cost per vaccine dose is US\$ 10.5. The main cost drivers in both urban and rural areas are personnel wages and vaccines (Table 4, paper II).

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The management of childhood pneumonia at the outpatient visit costs US\$ 3.2, and US\$ 6.6 per visit in urban and rural areas respectively. The urban/rural weighted unit cost per visit is US\$ 5.4 (Table 5, paper II). Inpatient bed days for children with severe pneumonia costs US\$ 45.2 in urban areas, and US\$ 63.5 in rural areas (Table 6, paper II).

### 8.2.2 Cost effectiveness

The base-case incremental cost-effectiveness analysis indicated that the 13-valent pneumococcal vaccine was more cost-effective with an ICER of US\$ 245 per LY gained and US\$ 258 per QALY gained compared to a strategy of no vaccine and PCV10 vaccine (Table 8, paper II). Both vaccines are highly cost-effective.

Rolling out pneumococcal vaccine to 93% coverage reduces direct and indirect medical care costs (Table 8, paper II). The vaccine further reduces the burden of pneumococcal infections caused by pneumonia, meningitis, bacteraemia and AOM (Table 7, paper II).

## 8.3 Paper III

Increased national coverage of key maternal and child health interventions to similar levels across geographical areas and between different socio-economic groups for a five year period would significantly improve the health outcomes of the worst-off population (mothers and young children). Increasing intervention coverage to equal levels across quintiles would reduce inequality in maternal and child mortality. Inequality in maternal and child mortality was reduced from a pro rich concentration index of  $-0.11$  to  $-0.03$  for maternal mortality and  $-0.12$  to  $0.03$  for child mortality. Reduction of maternal mortality was eight times higher in rural areas compared to urban areas, similar trends were observed in child mortality, the reduction in rural areas was five times greater than in the urban areas.

## 9.0 Discussion

Decisions on efficient and fair allocation of scarce health care resources remain a challenge in many developing health systems. In this thesis it has been demonstrated that the introduction of rotavirus vaccine alongside the current diarrhoea treatment is highly cost-effective compared to diarrhoea treatment given alone and that the introduction of pneumococcal vaccines in low-income settings is cost-effective and may reduce the burden of pneumococcal diseases. The scale up of priority maternal and child health interventions to the same levels would potentially save more lives in the poorest populations, and accelerate equitable progress towards improving maternal and child health. In conducting our study we encountered various methodological challenges. We will start by discussing key challenges and the various attempts to minimise any potential bias.

### 9.1 Methodological considerations

The three studies constituting this thesis have largely employed modelling techniques. The models require some assumptions and extensive data often obtained from different sources. In what follows I discuss the internal and external validity of our findings, the first two papers on cost-effectiveness are discussed together, and lastly I discuss the third paper on equity impact analysis.

#### 9.1.1 Internal validity

Internal validity refers to the extent to which the study results represent the actual target population [98]. Potential sources of biases that can impact on the internal validity of a study may be classified into three main groups; selection bias, information bias and confounding [98]. We further discuss other methodological issues unique to modelling techniques.

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## *Papers I and II*

### *Selection bias*

Selection bias arises when there is improper selection of the study subjects so they might not be representative of the actual study population [98, 99]. In cost-effectiveness and modelling studies the potential sources of selection bias may include exclusion of key costs or benefits, inadequate selection of alternative interventions for comparisons, and the use of effectiveness data that do not represent the study population [100].

### **Costing**

The cost for treatment of pneumonia, diarrhoea and the roll out of the pneumococcal and rotavirus vaccines among children under-five years were collected from only two regions of Tanzania. We collected data representing the urban rural divide. We involved a mixture of health care delivery, primary health care (health centre) and secondary health care (district hospital). To ensure that all relevant cost data were included, the pathway of a child seeking treatment for diarrhoea, pneumonia or vaccination was followed from entry into the health facility to exit after receiving the health care services. A structured checklist was used to identify, measure and value all resources consumed. Economic costs of donated or subsidised resources e.g. donated vaccine or volunteer personnel were included to ensure that the full economic cost of providing the services was determined.

We collected cost data from the health provider perspective; this might have underestimated the cost of child immunisation, diarrhoea and pneumonia treatment. Studies in Tanzania have shown that families incur out-of-pocket expenditure to access health care services, such as transportation, food and buying medicines [101, 102]. The exclusion of indirect and some direct costs paid by families may have hampered the estimation of the actual intervention cost, and the resources that might be saved by implementing the interventions e.g. vaccines. The choice of a health provider perspective may pose some limitations on the internal validity of our results. To minimise this, in paper II we chose a wider perspective and included patient costs. We used the average Tanzania GDP per capita and estimates of time lost from work

for patients of working age or time lost from work for parents of sick children to estimate the cost of productivity loss due to pneumococcal-related illness. The estimates might not represent the actual average annual income, but provided a glimpse of resources lost due to pneumococcal diseases and the potential resource gain associated with universal vaccination with PCV10 or PVC13 vaccines.

### **Intervention effectiveness**

We employed efficacy data retrieved from systematic reviews and meta-analysis of clinical trials. The estimate values for intervention efficacy used in our studies were from systematic reviews of clinical trials usually conducted in settings with higher quality of medical care. Therefore, achieving similar results in the community during implementation will depend on adherence to high quality health care services, which may not be available in some parts or levels of service in Tanzania. This could hamper the internal validity of our results; employing context specific data from community based clinical trials would be the ideal solution, but such data were not available for our setting.

The effectiveness data employed in our studies did not have direct head to head comparisons of the competing interventions. There were no systematic reviews with network meta-analysis; absence of the network meta-analysis may have an influence on the precision of our study results. Ideally network meta-analysis may have improved the accuracy of the model results and, hence minimise the potential bias of using effectiveness data from several different sources [103]. However, conducting independent network meta-analysis was beyond the scope of our study.

### ***Information bias***

Information bias occurs where there are systematic errors in the measurement of observations or responses during data collection [98]. The collection of cost data was the most likely source of information bias in our studies since the data were collected retrospectively. In most cases we required key informants to recall information relevant for the study population's medical pathway. More frequently, we relied on information from record books which in Tanzania, like in many other sub-Saharan countries, are not always kept accurately. We used standardized questionnaires to

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minimize possible information bias. Interviewers were trained and supervised to ensure that uniform and appropriate identification and measurement of all resources were used. It is usually a challenge to balance the demands for ensuring correct cost data for the relevant time, for example one year, and minimizing the recall period as much as possible. Collecting costing data prospectively by following children during immunisation, hospital visits or hospitalisation would have improved data quality and assisted in minimising the recall bias, but we didn't have time or resources to conduct such a resource-demanding prospective study.

### *Confounding*

Confounding occurs when the relationship between dependent and independent variables is explained by a third explanatory variable [104]. Costs and effectiveness may not be the only variables in economic evaluation models [105]. Other explanatory variables in a Markov health state, such as disease severity may influence the overall results. Diarrhoea and pneumococcal diseases have different levels of severity and this could have an impact on the cost and effectiveness. To some extent, we reported our cost data on the basis of known levels of severity to improve the internal validity. Generally, as explained above, the model parameters such as transition probabilities, effectiveness data etc. are derived from different sources and settings, with varying levels of uncertainty which may include inherent confounding effect. This may have some influence on the overall model results. The common approach in model based cost-effectiveness analysis does not directly adjust for confounders [106]. We assumed that in case the secondary data we used had inherent confounders, the potential impact of confounders on the model results would be accounted for in sensitivity analysis. Therefore we cannot rule out with certainty the influence of confounding variables on the model results.

### *Other potential sources of bias in economic evaluation*

Some specific factors could impact on the internal validity of the study outcome such as the appropriateness of the model structure to the study question or disease condition, or inadequate handling of uncertainty [100, 107].

### **The model structure**

The structure of an economic evaluation model is an important determinant of the model outcome and its applicability in decision making. Therefore consideration of the disease condition, its natural history, the policy question, and data availability guides how the model is structured. It is a common saying in the economic literature that “*all models are wrong*”...*but some models are useful*” [55]. The saying is motivated by the simplifications which are inherent in any modelling activity to enable easy interpretation. In other words, the assumptions and simplifications built into models will always have implications for the validity of the results. To increase internal validity, in papers I and II we employed Markov models that allow for the accounting of recurrent events, which are a common feature in infectious diseases. The cycle length and time horizon of the models were set to reflect the underlying diarrhoea and pneumococcal disease processes.

### **Handling of uncertainty**

Economic evaluation models involve information from a wide range of sources; uncertainties in these studies are inevitable. Data used in the model could be a source of flaw in the model outcome. To acknowledge the implications of various assumptions and to convey them into the uncertainty associated with the adoption of interventions, we employed one-way and probabilistic sensitivity analyses in papers I and II to ascertain the robustness of our results and to strengthen the internal validity. Chapter 2.7 of this thesis provides details of the procedures we employed in conducting sensitivity analysis.

### ***Paper III***

The LiST model combines complex demographic, epidemiological and efficacy data into a simplified model preloaded with country specific data such as fertility rates, age-specific mortality, intervention coverage, and efficacy results to allow easy use and interpretation. However, the model uses effectiveness data from several countries. There are few specific efficacy data for Tanzania, and this could limit the internal validity of our results. We made several attempts to contextualise and update the model with current intervention coverage and target rates from Tanzania. We

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conducted subgroup analysis by populating the model with urban/rural and wealth quintile specific data for Tanzania wherever possible. We were not able to test the robustness of the model results. When we used the LiST model, the sensitivity analysis module was not incorporated, and this may limit the extent to which we can be certain about the internal validity of our model results.

### 9.1.2 External validity

#### *Papers I and II*

External validity refers to the ability to generalize the study findings from the study area to other settings [98]. The cost data were collected from only two purposively selected regions of Tanzania and might not adequately represent the whole of Tanzania. Ideally we should have employed random sampling methods, such as cluster sampling [108], and included more regions to ensure wider representation of health care delivery in Tanzania. This was not done because of resource and time limitations. To some extent, that limits the generalisation of the cost data to the whole of Tanzania or other contexts.

The selected interventions might not be exhaustively representative of a wide range of alternatives available for the prioritised disease domains. However, for the purpose of creating a manageable model relevant to the study aim, we included what we considered to be key alternative interventions to allow appropriate comparison. The information on diseases in our study depends on context specific epidemiology. In extrapolating our results to other settings careful consideration should be made of the suitability of the chosen interventions. Our models are transparent and easy to populate with context specific information if deemed necessary.

Presentation of cost-effectiveness results may have an impact on the external validity of the study findings. Firstly, failure to adhere to the standardised guideline on reporting cost-effectiveness results, such as explaining the choice of perspective, comparators, time horizon, health outcome measure and the discount rates, may limit how far decision makers and other interested parties can interpret the results. Secondly, limitations may rise from the reporting of average cost-effectiveness ratios,



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the ratios limit comparison between the alternatives being evaluated [100]. To avoid these limitations, we attempted to adhere to economic evaluation reporting guideline [109]. Our findings on the alternatives under comparison were reported using incremental cost-effectiveness (ICER). This allowed us to determine the cost associated with moving from one intervention to the other and the related health outcomes, making it easy to compare alternatives. We further characterised the robustness of the model results by conducting one-way and probabilistic sensitivity analysis, and reporting the results of the sensitivity analysis. Chapter 2.6 presents details of the methods we applied in presenting and interpreting our results.

### *Paper III*

In paper III we reported the health outcomes following the rollout of key maternal and child health interventions. The LiST model may overestimate mortality reductions. The intervention efficacy used in the model may not necessarily represent the actual intervention effectiveness during implementation. The quality of services in Tanzania and in many other developing countries is below the quality of services offered by the clinical trials that provided the efficacy values. This may be the key limitation to the generalizability of our study findings, since we cannot guarantee with certainty that the quality of service in Tanzania will improve to the levels offered by the clinical trials.

Our results in paper III lack information about (marginal) cost. The version of the LiST model which was available did not have a costing component; this may limit the decision-making process using the results, especially the budget impact of rolling out the intervention. The LiST model has recently been developed further to include a costing module that may facilitate determining the costs of scaling up these interventions [110]. The LiST model used in this paper was tailored to a Tanzanian setting; therefore extrapolating our study findings to other settings may require populating the model with country specific data.

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## 9.2 Discussion of the main findings

### 9.2.1 Cost-effectiveness papers I and II

The findings of this study suggest that adding rotavirus vaccine to the current IMCI treatment of diarrhoea is highly cost-effective. Studies from other settings in sub-Saharan Africa have shown similar findings [111-113]. Children with access to both rotavirus vaccine and diarrhoea treatment will achieve more health benefits compared to those with access to either diarrhoea treatment with ORS or rotavirus vaccine alone.

Pneumonia and diarrhoea are leading causes of mortality in children under five years in Tanzania, and are responsible for over 18000 and 10000 annual deaths, respectively [114]. The introduction of immunisation against rotavirus and pneumococcal disease in Tanzania may substantially reduce the amount of premature mortality and prevent severe diarrhoea [115] pneumonia, AOM and invasive pneumococcal diseases [116-118].

According to our findings, the costs of delivering vaccine in rural areas are higher than in urban areas. In case of scarce resources, common to many developing countries health systems, it might be compelling to target easy-to-reach and less expensive urban areas, but this may potentially escalate the existing disparities. Further research, deliberation and debate on the normative arguments, are critical in exploring the distributive impacts of alternative policies. Our results have demonstrated that providing universal pneumococcal vaccine to all children in Tanzania is highly cost-effective, at a cost per QALY gained below one times GDP per capita for Tanzania. Previous findings from high income countries [119, 120], middle income countries [121], and more recently in low income countries [122] corroborate our findings.

However, introduction of a vaccination programme may offer additional benefits to families and the health system. Previous studies have indicated that roll out of a universal vaccination programme is likely to provide wider economic benefits, by

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reducing treatment costs and increasing productivity [123]. Similarly, findings from paper II have indicated that vaccines, if universally scaled up, may prevent illnesses and save family direct and indirect medical expenditures.

Using the framework on priority setting, the roll out of rotavirus vaccine for diarrhoea control and pneumococcal vaccine for preventing pneumococcal diseases qualifies for classification into the high priority category. Firstly, papers I and II have indicated that rotavirus and pneumococcal vaccines are highly cost-effective based on a threshold of less than one times the Tanzania (2012) GDP per capita of US \$610 [57]. Secondly, the root cause of diarrhoea and pneumonia is poverty, so they mainly affect the poorest population [124]. Therefore the interventions in the two papers address the health needs of the worst-off populations. Thirdly, the interventions offer financial risk protection through reduction in direct medical costs and reduction in indirect costs associated with seeking health care and absence from work.

### 9.2.2 Equity analysis Paper III

The results of paper III indicate that ensuring equal levels of access to maternal and child health interventions across socio economic quintiles and geographical divides will reduce inequality and prevent premature mortality. In our findings we have demonstrated that investing in the scale up of a minimal essential maternal and child health interventions to the national targets will reduce inequality and improve maternal and child health. Consequently, the population in rural areas, who currently have the least access, will reduce maternal mortality by about eight times and child mortality by about five times compared to affluent urban areas. Our findings corroborate previous findings that universal health coverage of maternal and child health interventions will improve health for the worst-off populations [125, 126]. Edging towards the end of the MDG target in 2015, there are still sizeable inequalities in access to maternal and child interventions in developing countries [127]. This is both inefficient and inequitable. In the discussion of the post 2015 agenda for new development goals, it has been suggested that *equitable* coverage of maternal and child health interventions is accelerated [128, 129]. Our results in paper

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III offer one example of a fair and efficient pathway for scaling up maternal and child health interventions.

Development of evidence-based policies and strategies on maternal and child health priorities is an important step in allocating resources, but might be insufficient if maternal and child health services are not appropriately delivered. Equitable access to quality maternal and child health services must be ensured. The strengthening of waivers and exemption schemes meant for mothers and children younger than five years is crucial to prevent catastrophic health expenditure through out-of-pocket payments for health services. In Tanzania it has been reported that families spend a considerable amount of resources on otherwise “free” health services for mothers and young children [101, 130, 131]. Universal access to essential health care services through universal health coverage safeguards families, particularly the worst-off, against destitution. In setting priorities, interventions that bring financial risk protection, are highly cost-effective, and target the worse off should be given considerable weight [89].

### 9.3 Policy implications

To ensure that everyone has equal access to priority health interventions, the government needs to invest in the health system. Using a priority setting framework proposed in this thesis, a minimum package of national priority maternal and child interventions could be developed and should form the basis of health systems strengthening. The incremental costs incurred in the implementation of the selected interventions will likely offset the finite health care budget; this will require trade-offs between services within the health system and increased health care funding.

The LiST tool is now included as a module in the new United Nations health strategic planning tool called One Health [110]. In its current form the One Health tool may be used for intervention costing, assessing budget impact and the associated fiscal space, due to expanded coverage of a mix of interventions. The methods may be used in formulating national medium-term health plans, through analysing the costs of

implementing alternative interventions, for example, the costs of expanding services selected in the high-priority category to a certain level of coverage. If the available budget is not exhausted, then the cost of implementing medium-level interventions will be estimated and the budget impact analysed. The process is ongoing until the budgeted resources have been exhausted [132, 133]. The mix and coverage of interventions may change or increase gradually depending on the health care budget set aside during the implementation period of the medium-term plan, usually five to ten years.

Evidence-based priority setting and resource allocation are central in strengthening health system performance and attainment of the universal coverage goals [134]. Investing in cost-effective and high-impact health interventions will facilitate equitable health care resource allocation and save maternal and child lives.

## 9.4 Research implications

Context specific cost-effectiveness evidence for Tanzania is developing; however more evidence is needed to enable fair and efficient priority-setting processes. There is a need to generate country-level evidence on cost-effectiveness, and equity impact of health interventions through local research [26]. The available information from surveys such as Health Information Management System (HIMS) and demographic and health surveys can be used to analyse existing inequalities in the health system. This will enrich priority-setting processes by incorporating the status of inequality in health and health care and the possible remedy. The information could be used for monitoring and evaluation of the progress of implementing the prioritised interventions. Capacity building of local institutions, researchers and enhancing collaboration and information exchange between institutions, could be one step towards self-sufficient health technology assessment and priority setting in Tanzania. Establishing new and stronger institutions for health technology assessment and priority setting is another and probably better option [26].

A comprehensive and effective priority-setting process requires the country to create institutions that can link evidence to priority-setting and implementation of the developed minimum package of essential maternal and child health interventions. Such an institution would coordinate different actors in the Tanzania health system such as the Ministry of Health, Ministry of Local Government, research institutes, non-governmental organisations and development partners. The coordination would ensure that priority setting is an ongoing process, create demand for more evidence, stimulate more research into cost-effectiveness and equity, and hence move the system towards achieving stated policy goals.

## 9.5 Conclusion

This study has shown that it is possible to use currently available methods and tools to generate evidence for policy decisions in low-income settings. Combining available information on the burden of disease, economic evaluation and equity analysis to develop evidence-based health policy and plans to ensure fair and efficient resource allocation is now possible, but remains a challenge. The use of scientific evidence to inform policy debates in prioritising health interventions is an important element in priority setting. Evidence-informed policy decisions are likely to be acceptable and move the system towards the goal of universal access to health services regardless of need.

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## **Papers I-III**







RESEARCH

Open Access

# Cost-effectiveness of live oral attenuated human rotavirus vaccine in Tanzania

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## Abstract

**Background:** Globally, diarrhoea is the second leading cause of morbidity and mortality, responsible for the annual loss of about 10% of the total global childhood disease burden. In Tanzania, Rotavirus infection is the major cause of severe diarrhoea and diarrhoeal mortality in children under five years. Immunisation can reduce the burden, and Tanzania added rotavirus vaccine to its national immunisation programme in January 2013. This study explores the cost effectiveness of introducing rotavirus vaccine within the Tanzania Expanded Programme on Immunisation (EPI).

**Methods:** We quantified all health system implementation costs, including programme costs, to calculate the cost effectiveness of adding rotavirus immunisation to EPI and the existing provision of diarrhoea treatment (oral rehydration salts and intravenous fluids) to children. We used ingredients and step down costing methods. Cost and coverage data were collected in 2012 at one urban and one rural district hospital and a health centre in Tanzania. We used Disability Adjusted Life Years (DALYs) as the outcome measure and estimated incremental costs and health outcomes using a Markov transition model with weekly cycles up to a five-year time horizon.

**Results:** The average unit cost per vaccine dose at 93% coverage is US\$ 8.4, with marked difference between the urban facility US\$ 5.2; and the rural facility US\$ 9.8. RV1 vaccine added to current diarrhoea treatment is highly cost effective compared to diarrhoea treatment given alone, with incremental cost effectiveness ratio of US\$ 112 per DALY averted, varying from US\$ 80–218 in sensitivity analysis. The intervention approaches a 100% probability of being cost effective at a much lower level of willingness-to-pay than the US\$609 per capita Tanzania gross domestic product (GDP).

**Conclusions:** The combination of rotavirus immunisation with diarrhoea treatment is likely to be cost effective when willingness to pay for health is higher than USD 112 per DALY. Universal coverage of the vaccine will accelerate progress towards achievement of the child health Millennium Development Goals.

**Keyword:** Cost, Cost-effectiveness, Rotavirus, Vaccine

## Background

Diarrhoea is the second leading cause of morbidity and mortality globally among children below five years of age and is responsible for 23 million Disability Adjusted Life Years (DALYs) annually, about 10% of the total global childhood disease burden [1]. The global burden of diarrhoea is highest among children in low-income countries, with countries in sub-Saharan Africa accounting for more than 50 per cent of cases worldwide [1]. In Tanzania, about fourteen per cent of all deaths in

children younger than five years is due to diarrhoea, making it liable for five per cent of the total national DALYs [1,2]. About 70 per cent of the burden occurs before the first birthday. Tanzanian children under the age of five, are estimated to have 3.5 episodes of diarrhoea per year, reaching a peak frequency between 6–12 months of 4.72 episodes per year [3]. Rotavirus is the single most important cause of diarrhoea: estimated to represent about 40 per cent of all diarrhoea related morbidity and mortality in children globally [4]. Similar diarrhoea causality has been observed in a multi-country study, which included Tanzania, where 34 percent of all diarrhoea episodes were due to rotavirus [5].

The introduction of integrated management of childhood illness (IMCI) more than two decades ago strengthened the

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management of diarrhoea [6], with the adoption of oral rehydration solution (ORS) as a main intervention for diarrhoea treatment, recommended by World Health Organization (WHO) and United Nations Children's Fund (UNICEF) [7]. Treatment of diarrhoea with ORS has shown marked effectiveness in preventing dehydration and reducing diarrhoea related mortality [8]. To achieve optimal effectiveness, diarrhoea treatment adopting the principles of IMCI requires large coverage and community participation. However, the recent emphasis on vertical programmes, targeting specific diseases such as Malaria, TB and HIV/AIDS, has led to reduced funding for IMCI and has weakened the management and control of diarrhoea [9].

WHO recommends including rotavirus vaccine into national immunization programmes [10]. Tanzania did this under the support of the GAVI Alliance in January 2013 [11]. Two rotavirus vaccines are currently available for Tanzania. Rotarix®, by GlaxoSmithKline, is a single strain, live attenuated human rotavirus vaccine (RV1) administered orally in two doses. RotaTeq™ by Merck & Co Inc., is a live, human-bovine reassortant pentavalent rotavirus vaccine (RV5), administered orally in three doses. A third vaccine LLR, Lanzhou Institute Biomedical Products is a three dose vaccine currently licensed for use in China only, while a fourth Indian vaccine (ROTAVAC), has shown promising results but is not yet available for scale up [12]. WHO recommends that infants are vaccinated between six and fifteen weeks, and that the last dose is not given later than 32 weeks of age [13,14]. The introduction of RV1 in Tanzania offered a unique opportunity to quantify all health system implementation costs, including programme costs, during planning, piloting and scale-up of the new programme. The aim of this study was to collect primary cost data from the perspective of the health care provider and to compare the cost-effectiveness of the RV1 rotavirus vaccine to existing treatment strategies for diarrhoea in children.

## Methods

### Study setting and perspective

The study was a cost effectiveness analysis from the perspective of health service providers in Tanzania. We adopted a health provider perspective because this information would be important for national health decision makers, and because a wider societal perspective is much more data intensive and would require data that are not easily available in this setting. We compared the current treatment of diarrhoea (using oral rehydration salt (ORS) and intravenous (IV) fluid), with the addition of rotavirus vaccination to the current diarrhoea treatment and with the provision of rotavirus vaccine (RV1) alone. In addition we included a hypothetical alternative

of providing no treatment to reflect further on what the outcome might be if the interventions were not implemented [15]. The pentavalent rotavirus vaccine (RV5) strategy was not included in the model analysis due to lack of cost data in Tanzania.

### Description of interventions

Treatment of diarrhoea in children with ORS and IV fluids in Tanzania follows a three-step plan (A-C) depending on diarrhoea severity, which is determined by dehydration status. Plan A should be followed for cases of mild diarrhoea, plan B for moderate and plan C for severe diarrhoea [16]. The single strain live attenuated human rotavirus vaccine (RV1) is administered to infants orally in two doses, the first dose at six weeks and the second at ten weeks [14].

### Costs

We collected primary cost data for diarrhoea management and additional costs of introducing RV1 to the national immunisation programme in two districts, purposely sampled to include a rural district (Kisarawe) and an urban district (Ilala). Costing was done from a health provider perspective. In each district we collected data from one hospital (Amana hospital for Ilala and Kisarawe hospital for Kisarawe district) and one health centre (Chanika Health Centre in Ilala and Masaki Health Centre in Kisarawe) for the one-year period July 2011 to June 2012. We collected the cost data before the introduction of rotavirus vaccine, but the preparation for the rollout was at an advanced stage, including plans for the procurement and distribution of vaccines, training of health personnel and the preparation for storage facilities. In case the available information on resource use was not sufficient we used information on other vaccines under the expanded programme on immunisation (EPI). We used a modified WHO and Joint United Nations Programme on HIV and AIDS (UNAIDS) costing tool, to identify all resource use [15,17].

### Resource identification

We categorised health facility departments into three costing centres and applied the ingredient approach as proposed by WHO-CHOICE to identify resource use in each of the cost centres [15]. First, we identified all resources used in centres that directly provide services for child immunisation, and outpatient and inpatient departments that provide diarrhoea treatment to children. Second, we identified resources used in indirect care cost centres that provided services but not direct medical care (ancillary services). Thirdly, we included other support service cost centres such as general administrative and warehouse costs.

### Resource measurement and valuation

Resource use was categorised into recurrent and capital goods. We classified capital items as those with useful life years above one year or costing above Tsh100000 (about 62 US\$). Resource use was measured through review of available inventories such as ledgers, order books, and records of medical supplies used. All records were anonymous, only specifying resources used in treating diarrhoea or providing rotavirus vaccine. We employed a step down costing approach to allocate resources between cost centres [18]. The proportion of the number of workers at each cost centre as a percentage of total workers at the health facility was used to allocate shared resources to the cost centres. The number of diarrhoea patients among all inpatient and outpatient attendees, and the number of rotavirus doses as a percentage of all vaccine doses were used as a proxy to obtain specific resource use by each intervention.

To value all identified resources for rotavirus vaccination and diarrhoea management, we used the Tanzania Medical Stores price catalogue to assign costs for medical equipment and drugs [19]. The cost of non-medical equipment was obtained from 2011/2012 tender prices for the Government Procurement Services Agency (GPSA) [20]. Building rents were estimated as per Tanzania National Housing Corporation (NHC) rental charges obtained through interview with key personnel at NHC. All cost data were collected in Tanzania shillings (TSH) and converted to US dollars using the Bank of Tanzania Interbank average annual exchange rates for 2011 and 2012 [21].

The capital costs were annuitized using Bank of Tanzania average interest rates for 2011/ 2012 at 9.6 per cent [21], and we adopted useful life years from WHO country estimates [22]. All data were analysed using Microsoft Excel (2010).

### Unit cost

To obtain the unit cost per immunized child, we divided the total cost by the total estimated number of children to be vaccinated with the RV1 vaccine, obtained from the current coverage levels of the existing child immunisation package (DPT- HB) from each of the study facilities. Outpatient (OPD) unit costs were obtained by dividing the total OPD cost (capital and recurrent cost) by the annual number of children with moderate diarrhoea visiting the OPD. Inpatient (IPD) unit costs were derived by dividing the total IPD cost (capital and recurrent cost) by the total number of IPD bed days specific to children admitted with severe diarrhoea. To obtain the total unit cost, the urban/rural costs were weighted using the proportion of population attending at each health facility, and the proportion of the population in each district. We assumed the constant returns to scale, i.e. the same unit prices for administration

and disease management apply both with and without the intervention.

### Effectiveness

Through a systematic search we identified the most recently updated systematic reviews and meta-analyses of the effectiveness of the RV1 vaccine [14]. Only one multicentre double blinded, randomized placebo-controlled study conducted in South Africa and Malawi [23], reported rota vaccine efficacy on all-cause diarrhoea for countries with high diarrhoea mortality rates. The data analysis was conducted according to the protocol. The efficacy from this trial is used in our study. The effectiveness of diarrhoea treatment using ORS was retrieved from a systematic review by Munos et al. [24]. The effectiveness of IV fluids against severe diarrhoea were obtained from a Cochrane systematic review by Hartling et al. [25]. In our model we used vaccine efficacy against all-cause severe diarrhoea to reflect the real Tanzanian clinical settings whereby routine management of diarrhoea is based on clinical assessment criteria. Key input parameters are listed in Table 1.

### Markov model overview

We constructed an individual Markov state-transition model (Figure 1) with weekly cycles with TreeAge Pro 2013 software (Williamstown, MA, USA). A five-year time horizon was adopted to reflect the fact that diarrhoea from rotavirus infection is primarily a health problem during the first five years of life [3,5,10].

For each weekly cycle in the model, children can be in one of four possible health states; well/asymptomatic infection (1), moderate diarrhoea (2), severe diarrhoea (3) and dead (4). Children in the well/asymptomatic state are exposed to diarrhoea infections. For each cycle, the child may remain well, contract moderate diarrhoea or die from other causes (background mortality). In the moderate state, children may recover from diarrhoea infection, continue with recurrent moderate diarrhoea, progress to severe diarrhoea or die from other causes. Individuals progressing to severe diarrhoea may recover, continue with recurrent moderate diarrhoea or die from either diarrhoea or other causes. The model assumptions were based on the diarrhoea classification by severity described in the Tanzania national treatment guideline [16].

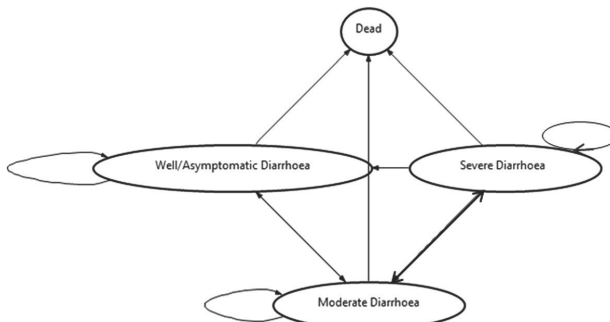
### Transition probabilities

The movement between health states (as described above) is modelled on the basis of transition probabilities and the effectiveness values of the diarrhoea treatment options in the model. The probabilities were obtained from the literature. The probabilities of acquiring moderate diarrhoea infections are based on age specific incidence for Tanzania (Table 1) [3]. Yearly

**Table 1 Key input parameters for cost-effectiveness base case and sensitivity analyses**

Parameter	Base case	Range	Distribution	Source
<b>Cost (2012 US\$)</b>				
Cost per fully immunised child for rota vaccine (RV1) at 93% coverage (cRotaVac)**	16.99	±25%	Gamma	Table 2
Cost per OPD visit for diarrhoea treatment (cModD)	3.84	±25%	Gamma	Table 3
Cost of in-patient diarrhoea treatment per bed day (cSevD)	8.90	±25%	Gamma	Table 4
Cost discounting rate (cDR)	0.03	0.00 – 0.06	N/A	[15]
<b>Disability weights</b>				
Disability weight moderate Diarrhoea (uModD)	0.202	0.133 - 0.299	Beta	[32]
Disability weight severe Diarrhoea (USevD)	0.281	0.184 - 0.399	Beta	[32]
Outcome discounting rate (oDR)	0.030	0.000 – 0.060	N/A	[15]
<b>Effectiveness (Relative Risk ratio)</b>				
Effectiveness of RotaVaccine on all cause diarrhoea (effRotaVac)	0.698	0.570 - 0.850	Log-normal	[23]
Effectiveness of IMCI on moderate diarrhoea (effImci_OPD)	0.590	0.430 - 0.680	Log-normal	[24]
Effectiveness of IMCI on severe diarrhoea (effImci_IPD)	0.570	0.420 - 0.660	Log-normal	[25]
<b>Transition Probabilities (weekly)</b>				
Probability of progressing from well to moderate diarrhoea (tpModD)	0.116	0.072 - 0.167	Beta	[3]
Probability of progressing from moderate to severe diarrhoea (tpSevD)	0.048	0.035 - 0.056	Beta	[27]
Probability of recurrent moderate diarrhoea (tpRecModD)	0.005	0.004 – 0.006	Beta	[28]
Probability of recurrent severe diarrhoea (tpRecSevD)	0.0038	0.003 – 0.0045	Beta	[28]
<b>Mortality</b>				
Probability of dying from diarrhoea (Case fatality rate (CFR) <5 yrs (%)) (PDeath_NoInt)	0.019	0.0119 -0.0265	Normal	[27]
<b>General</b>				
Average number of bed days spent in hospital	4	2 - 6	N/A	Primary data
Diarrhoea treatment coverage rates	41%	44%-68%	N/A	[30]
Vaccine coverage rates ( reference to DPT-HB-Hib coverage)	93%	85% – 95%	N/A	[30]
Healthy life expectancy at birth	52	49,4 - 53,1	N/A	[32]

\*\*In the model the vaccination cost are assigned once as transition cost to vaccinated child on first and second dose i.e. only during a monthly cycle corresponding to vaccination.



**Figure 1** Markov model showing the health states of diarrhoeal disease, including “well/asymptomatic”, “moderate diarrhoea”, “severe diarrhoea” and “dead”, which is an absorbing state.

incidence rates were converted to weekly probabilities of diarrhoea infections using the formula  $p = 1 - \exp^{-rt}$  where  $p$  = probability,  $r$  = rate,  $t$  = time period (weekly) [26]. The transition probability of progressing from moderate to severe diarrhoea is based on a systematic review by Walker et al. [27], while the probabilities of recurrent moderate and severe diarrhoea were taken from Lamberti et al. [28] (Table 1).

To estimate the likelihood of mortality from diarrhoea infection, case fatality rates (CFR) for diarrhoea were retrieved through a literature search [27]. We used a Tanzanian life table for the year 2011 to estimate the risk of all-cause mortality, which was adjusted for diarrhoea mortality to calculate background mortality rates [29]. We assumed a reasonable target coverage of rotavirus vaccine to be equal to DPT-HB vaccine coverage (93%) [30]. We applied a dropout rate of 5% for the second dose, on the basis of the 2010 Tanzania Demographic and Health Survey (TDHS) [30].

#### Health outcomes

We estimated health outcomes using disability-adjusted life years (DALYs). DALYs were calculated in the Markov model by combining years lived with disability (YLD) and years of life lost (YLL) for each weekly cycle. DALYs averted were calculated for each cycle and accumulated over the model time horizon. This was repeated for each diarrhoea management strategy [31]. DALYs averted were calculated as the difference between the treatment strategies. To obtain YLD, we used recently updated disability weights of 0.202 and 0.281 for moderate and severe diarrhoea [32]. For children in a well state a disability weight of 0 was applied, assuming all individuals in this state are either healthy or with asymptomatic diarrhoea [32]. We did not incorporate age weighting since this is not recommended in the most recent DALY guidelines [33].

To compute YLL, a disease weight of 1 reflecting the worst state (i.e., death) and a healthy life expectancy at birth for Tanzania, 52 years, was used [34]. All individuals in the state of death were assigned a weight of 1. At the final cycle all cohorts ending up in the state of wellness were assigned a final reward equal to the healthy life expectancy at two years [31].

#### Cost effectiveness analysis

We used the hypothetical no intervention as a baseline and compared it to the modelled incremental cost effectiveness ratios (ICERs) of implementing the current standard of care for diarrhoea treatment in children, adding the RV1 vaccine to the current diarrhoea treatment, and RV1 vaccine given alone. The base case ICER was computed by dividing the incremental cost to incremental DALYs averted in each of the study interventions. Costs and effectiveness were discounted at an annual rate of 3%

recommended by WHO for low income countries [15]. Most economic evaluation guidelines recommend discounting of both cost and effects, which is also reflected in the applied literature [18,35,36].

#### Sensitivity analyses

We performed one-way sensitivity analyses to evaluate the impact of single assumptions on costs and outcomes. As upper and lower variable ranges, we used upper and lower 95% confidence limits, respectively, wherever reported in the literature. When confidence intervals were not reported and for the primary cost data we used a range of  $\pm 25\%$  (Table 1). This reflects a reasonable range of variation in cost and is commonly used in cost effectiveness studies [37-39].

We used probabilistic sensitivity analysis to assess the overall robustness of the results. We did this by running the model with distributions for each parameter rather than point estimates. We computed distributions for the parameters using base case values as means, and standard errors calculated from uncertainty ranges (Table 1). For disability weights and transition probabilities, beta distributions were used since this restricts values to the range between 0 and 1. Gamma distributions were used for costs to avoid negative values [26], while, log-normal distributions were assumed for relative risks.

Monte Carlo simulation was used to draw 10,000 random samples from the distributions that were combined into cost-effectiveness pairs. The cost-effectiveness pairs were used to estimate the probability that each intervention is cost effective for a range of willingness to pay to avert DALYs. The results of the probabilistic sensitivity analysis are presented as a cost-effectiveness scatter plot and a cost-effectiveness acceptability curves.

#### Research ethics

Ethical clearance was obtained from Medical Research Coordinating Committee of the National Institute for Medical Research, Tanzania. All data used in the study were anonymous; only record books without any patient identity were used. The funding agency had no influence on the study design or results.

## Results

### Costs

The total weighted average cost of rolling out RV1 vaccine at 93% coverage is US\$ 8.4 per vaccine dose. The weighted unit cost per vaccine dose is US\$ 5.2 in urban health facility and US\$ 9.8 in rural facilities (Table 2). Recurrent costs account for 89% in urban and 87% in rural facilities. In urban facilities, 60% and, in rural facilities, 39% of the total cost is used for purchase and distribution of vaccines.

**Table 2 Average cost for providing rotavirus vaccine services, 2012 US\$**

Cost category	Urban						Rural					
	Hospital	%	Health Centre	%	Average	%	Hospital	%	Health Centre	%	Average	%
<b>Capital Cost, N (%)</b>												
Buildings	582	2.6	517	5.3	550	3.5	504	8.3	265	4.8	384	6.6
Equipment	234	1.1	210	2.2	222	1.4	163	2.7	147	2.7	155	2.7
Vehicles	140	0.6	140	1.4	140	0.9	36	0.6	33	0.6	35	0.6
Training on IMCI	281	1.3	249	2.6	265	1.7	236	3.9	189	3.4	213	3.7
<b>Total capital costs</b>	<b>1237</b>	<b>5.6</b>	<b>1116</b>	<b>11.5</b>	<b>1177</b>	<b>7.4</b>	<b>939</b>	<b>15.4</b>	<b>634</b>	<b>11.5</b>	<b>787</b>	<b>13.5</b>
<b>Recurrent Cost, N (%)</b>												
Personnel	7030	32.0	1188	12.3	4109	26.0	1997	32.8	1649	29.9	1823	31.4
Vaccine	12498	56.9	6477	67.0	9487	59.9	2197	36.0	2338	42.3	2268	39.0
Supplies	175	0.8	150	1.6	163	1.0	83	1.4	76	1.4	79	1.4
Vehicle operation and maintenance	56	0.3	56	0.6	56	0.4	52	0.9	32	0.6	42	0.7
Building operation and maintenance	468	2.1	18	0.2	243	1.5	59	1.0	15	0.3	37	0.6
Community sensitisation and Monitoring	516	2.3	671	6.9	594	3.8	658	10.8	658	11.9	658	11.3
Outreach	-	-	-	-	-	-	112	1.8	123	2.2	117	2.0
<b>Total recurrent costs</b>	<b>20743</b>	<b>94.4</b>	<b>8560</b>	<b>88.5</b>	<b>14652</b>	<b>92.6</b>	<b>5158</b>	<b>84.6</b>	<b>4891</b>	<b>88.5</b>	<b>5024</b>	<b>86.5</b>
<b>Grand Total</b>	<b>21980</b>		<b>9676</b>		<b>15829</b>		<b>6097</b>		<b>5525</b>		<b>5811</b>	
<b>Unit Cost</b>												
Number of doses administered	4041		2094				711		477			
Cost per dose at 93%	5.4		4.6		5.0		8.6		11.6		10.1	
% proportion of hospital/health centre administered doses	66 %		34 %				60 %				40%	
Weighted unit cost per dose	3.6		1.6		5.2		5.1		4.7		9.8	
<b>% proportion of urban/rural population</b>	<b>29 %</b>						<b>71%</b>					
Urban/rural weighted cost per dose					1.5						6.9	
<b>Weighted average cost (Urban/rural) per dose</b>					<b>8.4</b>							

Tables 3 and 4 present total and unit cost of diarrhoea management in urban and rural health facilities in more detail. The cost of managing a case of moderate diarrhoea is US\$ 2.9 per visit (Table 3) in urban facilities, and US\$ 4.2 per visit in rural facilities. Severe diarrhoea management costs US\$ 7.6 and US\$ 9.4 per bed day in urban and rural health facilities, respectively. Personnel remuneration is the major expenditure, consuming 62% in urban and 39% in rural facilities of the total cost for treating moderate diarrhoea. There is a similar trend for severe diarrhoea with personnel remuneration representing 64% and 42% of total expenditure for urban and rural facilities, respectively.

#### Cost-effectiveness

At baseline, providing only rotavirus immunisation is the least effective of the alternatives, with 1.4 DALYs averted per child, while diarrhoea management alone and vaccine plus diarrhoea treatment in combinations avert 2.0 and 2.5 DALYs per child respectively.

The vaccine alone is also the cheapest of the alternatives with a cost estimate of US\$ 59 per child, while the cost of diarrhoea treatment is US\$ 112 and the vaccine and treatment in combination is US\$ 167 per child. There is no dominance, and the incremental cost-effectiveness ratios (ICERs) are US\$ 43 and 112 per DALY averted when moving between the three alternatives (Table 5). Rotavirus vaccine in combination with diarrhoea treatment using ORS and IV fluids is therefore the most cost-effective option compared to the vaccine or diarrhoea treatment alone (Table 5), given that the willingness to pay is at least US\$ 112 per DALY.

#### One-way sensitivity analysis

The one-way sensitivity analysis indicates that the vaccine efficacy of diarrhoea is the most influential parameter in the base case analysis (Figure 2). Evaluating the model at the lower limit of the effectiveness of rotavirus vaccine on all cause diarrhoea (0.57), the ICER improved significantly from US\$ 112 to US\$ 80 per DALY averted,

**Table 3 Average outpatient cost diarrhoea treatment per visit, by location and level of service, 2012 US\$**

Cost category	Urban					Rural						
	Hospital	%	Health Centre	%	Average %	Hospital	%	Health Centre	%	Average %		
<b>Capital Cost, N (%)</b>												
Buildings	4016	12.3	84	12.2	2050	12.3	61	4.3	160	17.3	111	9.4
Equipment	362	1.1	5	0.7	184	1.1	9	0.6	16	1.7	12	1.1
Vehicles	446	1.4	27	3.9	237	1.4	22	1.5	0	0.0	11	0.9
Training on diarrhoea management	1328	4.1	269	39.0	799	4.8	802	56.6	72	7.8	437	37.3
<b>Total capital costs</b>	<b>6152</b>	<b>18.9</b>	<b>385</b>	<b>55.6</b>	<b>3268</b>	<b>19.6</b>	<b>893</b>	<b>63.0</b>	<b>248</b>	<b>26.8</b>	<b>571</b>	<b>48.7</b>
<b>Recurrent Cost, N (%)</b>												
Personnel	20371	62.4	204	29.5	10288	61.8	299	21.1	622	67.1	460	39.3
Drugs and Medical supplies	3879	11.9	63	9.1	1971	11.8	58	19.1	47	5.0	53	4.5
Supplies	284	0.9	13	1.8	148	0.9	72	5.1	9	0.9	40	3.4
Vehicle operation and maintenance	413	1.3	22	3.2	218	1.3	23	1.6	0	0.0	11	1.0
Building operation and maintenance	254	0.8	5	0.7	130	0.8	26	1.8	0	0.0	13	1.1
Cleaning and Laundry	1269	3.9	1	0.2	635	3.8	46	3.2	2	0.2	24	2.0
<b>Total recurrent costs</b>	<b>26470</b>	<b>81.1</b>	<b>308</b>	<b>44.4</b>	<b>13389</b>	<b>80.4</b>	<b>523</b>	<b>37.0</b>	<b>679</b>	<b>73.2</b>	<b>601</b>	<b>51.3</b>
<b>OPD Grand Total</b>	<b>32 622</b>		<b>693</b>		<b>16 657</b>		<b>1416</b>		<b>927</b>		<b>1171</b>	
<b>Unit Cost</b>												
Number of annual visit	11 277		247				305		249			
Cost per OPD visit	2.9		2.8				4.6		3.7			
% proportion of Hospital\health centre annual visit	98 %		2 %				55 %		45 %			
Weighted unit cost per visit	2.8		0.1		2.89		2.6		1.7		4.2	
% proportion of urban\rural population	29 %						71 %					
Urban\rural weighted cost per visit					0.8						3.0	
<b>Total weighted average cost per child treated</b>					<b>3.8</b>							

while the upper limit (0.88) predicted a higher ICER of US\$ 218 per DALY averted. Other parameters with substantial influence on model results were transition probabilities from well to moderate diarrhoea, diarrhoea case fatality rate, effectiveness of ORS on moderate diarrhoea treatment, transition probabilities from moderate to severe diarrhoea, and the effectiveness of IV fluids on severe diarrhoea treatment and the discount rate for health outcomes.

#### Probabilistic sensitivity analysis

The probabilistic sensitivity analysis (Figure 3) reveals the combined model uncertainty in cost and effectiveness, and shows that for the rota vaccine alone strategy, uncertainty is largely associated with effectiveness, while uncertainty varies more equally between costs and effectiveness for the diarrhoea treatment alone and the rotavirus vaccine plus diarrhoea treatment.

The cost effectiveness acceptability frontier (Figure 4) illustrates that willingness to pay to avert a DALY decides which intervention is likely to be most cost-effective. Until

willingness to pay to avert a DALY exceeds US\$ 40, the null intervention is optimal. For willingness to pay for health between US\$ 40 and 80 the vaccine provided alone has the highest probability of being optimal, while in the range US\$ 80 to 112 per DALY averted; diarrhoea treatment alone is most likely to be cost-effective. When willingness to pay exceeds US\$ 112 per DALY averted the combined strategy of providing both the vaccine and diarrhoea management is likely to be optimal.

Figure 4 also illustrates that there is a large degree of uncertainty surrounding these findings, especially regarding the ranges of willingness to pay for which the monotherapies may be considered optimal. In fact, both these recommendations have less than 60% probability of being cost effective. Uncertainty diminishes only when willingness to pay exceeds about USD 160 per DALY, after which the probability of the combined intervention being cost-effective is higher than 80%. Rotavirus vaccine and diarrhoea treatment combined approaches a 100% probability of being cost effective at a much lower level of willingness-

**Table 4 Average inpatient cost for diarrhoea treatment, by location and level of service, 2012 US\$**

Cost category	Urban				Rural					
	Hospital	%	Health Centre	Average	%	Hospital	%	Health Centre	Average	%
<b>Capital Cost, N (%)</b>										
Buildings	3066	12.9	-	3066	12.9	277	10.1	-	277	10.1
Equipment	408	1.7	-	408	1.7	49	1.8	-	49	1.8
Vehicles	74	0.3	-	74	0.3	92	3.4	-	92	3.4
Training on diarrhoea management	679	2.9	-	679	2.9	285	10.4	-	285	10.4
<b>Total capital costs</b>	<b>4227</b>	<b>17.8</b>	-	<b>4227</b>	<b>17.8</b>	<b>703</b>	<b>25.7</b>	-	<b>703</b>	<b>25.7</b>
<b>Recurrent Cost, N (%)</b>										
Personnel	15250	64.3	-	15250	64.3	1141	41.7	-	1141	41.7
Drugs and Medical supplies	1831	7.7	-	1831	7.7	163	5.9	-	163	5.9
Supplies	728	3.1	-	728	3.1	327	11.9	-	327	11.9
Vehicle operation and maintenance	30	0.1	-	30	0.1	98	3.6	-	98	3.6
Building operation and maintenance	550	2.3	-	550	2.3	111	4.1	-	111	4.1
Cleaning and Laundry	1111	4.7	-	1111	4.7	196	7.1	-	196	7.1
<b>Total recurrent costs</b>	<b>19500</b>	<b>82.2</b>	-	<b>19500</b>	<b>82.2</b>	<b>2036</b>	<b>74.3</b>	-	<b>2036</b>	<b>74.3</b>
<b>IPD Grand Total</b>	<b>23727</b>			<b>23725</b>		<b>2739</b>			<b>2738</b>	
<b>Unit cost</b>										
in-patient days	3103			3103		291			291	
Cost per in-patient day	<b>7.6</b>			<b>7.6</b>		<b>9.4</b>			<b>9.4</b>	
% proportion of urban\rural population	<b>29 %</b>					<b>71 %</b>				
Urban\rural weighted cost in-patient day			<b>2.2</b>					<b>6.7</b>		
<b>Total weighted (urban\rural) average cost per in-patient day</b>						<b>8.9</b>				

to-pay than the US\$609 per capita Tanzanian gross domestic product (GDP) in 2011/2012, suggested by the World Health Organisation as highly cost-effective [40].

## Discussion

This is the first published cost-effectiveness analysis for Tanzania comparing the potential benefit of rotavirus vaccine with diarrhoea management either in combination or if each intervention were implemented separately. We found that rotavirus vaccine provided as a package with diarrhoea treatment is highly cost-effective compared to the implementation of diarrhoea treatment alone or only providing RV1 vaccine. The incremental cost effectiveness ratio remained highly cost effective during sensitivity analysis. One way sensitivity analysis shows that for the most influential parameter i.e. the effectiveness of rotavirus

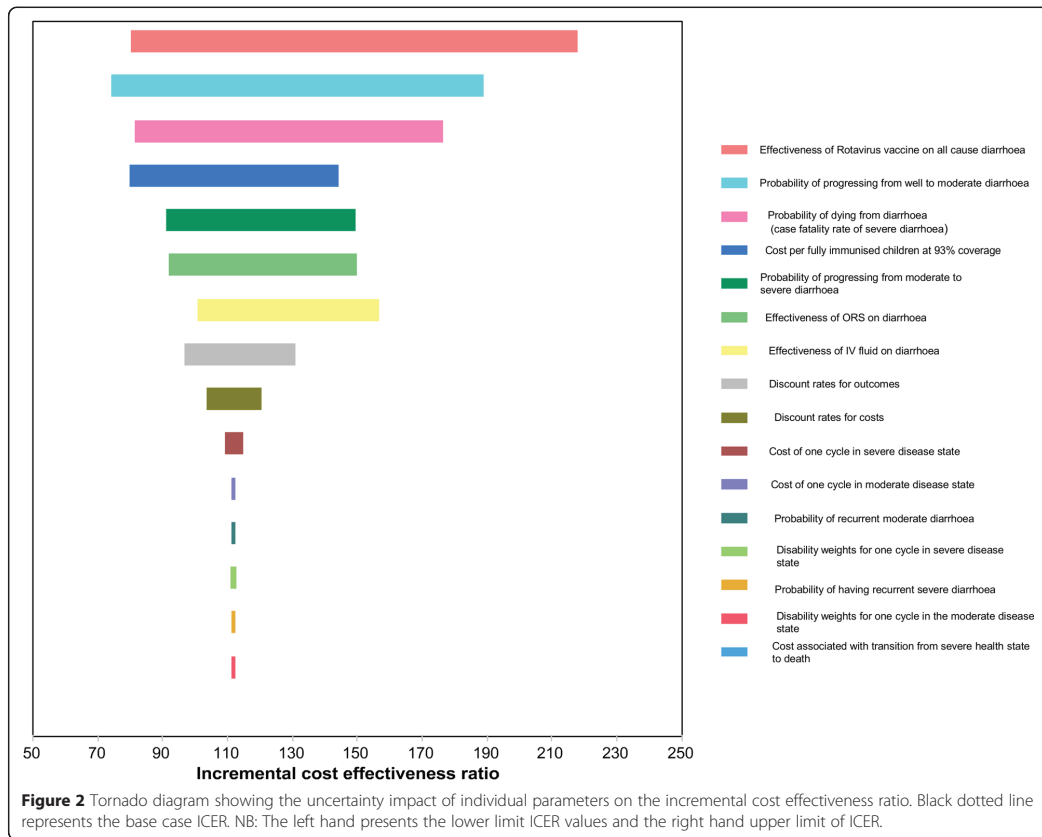
vaccine, the highest ICER is US\$ 237 per DALY averted which is lower than Tanzania's GDP.

The Tanzanian package of essential health interventions and the strategic plan for reduction of maternal and child mortality (2008 to 2015), recommends giving priority to interventions that are cost effective and address the major causes of morbidity and mortality [41,42]. Both policy documents recommend diarrhoea treatment with ORS as a key intervention in diarrhoea control. However, our study shows that diarrhoea treatment alone is likely to be less cost effective than combining it with rotavirus vaccination for reasonable levels of willingness to pay per DALY averted. These findings corroborate the current WHO recommendation on diarrhoea control, emphasising the provision of both prevention and treatment of diarrhoea as a package [10].

**Table 5 Baseline cost effectiveness results**

Strategy	Cost	Incremental cost	DALYs Averted	Incremental DALYs	ICER
<b>Discounted</b>					
No Intervention	0.0	0.0	0.00	0.00	0
Rotavirus Vaccine Alone	59.3	59.3	1.39	1.39	43
Diarrhoea Management	112.2	52.9	1.98	0.59	90
Rotavirus V& Diarrhoea Management	166.7	54.5	2.47	0.49	112



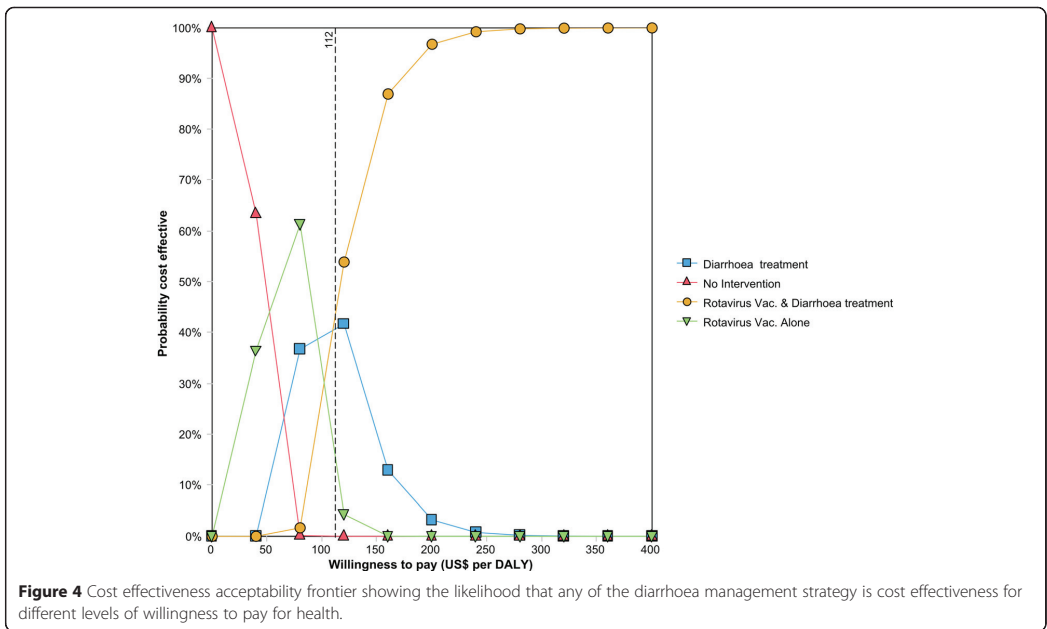
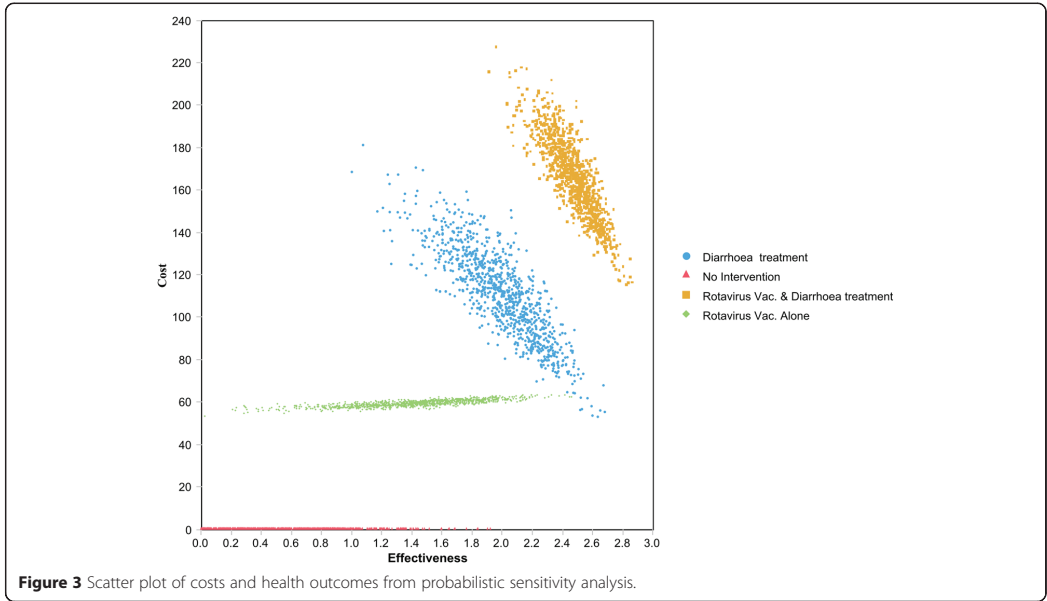


We cannot rule out the possibility that local variation in conditions, including epidemiology and capacity for service provision may influence the finding that diarrhoea treatment or vaccine provided alone is less cost effective, but these are unlikely to change the main finding that adding the vaccine is highly cost-effective.

At a unit cost between US\$ 5.2 (urban health facilities) to 9.4 in rural facilities per vaccine dose, estimated from subsidised GAVI alliance prices[11] in additional to administrative cost and vaccine wastage from primary cost data. Our study shows that it costs twice as much to deliver the vaccine in the rural facilities as in the urban facilities. This is primarily because there are fewer children in the rural area accessing health care services. Hence there are fewer patients to share the fixed capital costs and the fixed personnel costs of each facility (Figure 2). In other words, both vaccination and diarrhoea treatment are likely to be more cost-effective in urban than in rural areas. Since health services are generally better available and of higher quality in urban areas, this means that scale up of rotavirus

vaccination may represent an equity-efficiency trade-off. Prioritizing urban areas will allow more children to be immunized when funds are insufficient for full coverage, but at the same time this will further increase existing disparities. More empirical research is needed to explore the distributive impacts of alternative policies, coupled with deliberation and debate on the normative arguments.

The findings of our study are similar to previous studies on a two-dose monovalent RV1 vaccine in other low-income countries. A study from Malawi reported an ICER value of US\$ 75 per DALY averted at vaccine cost of US\$ 5.5 per dose [38]. Atherly et al. found a cost of US\$ 78 per DALY averted in the WHO AFRO region, at vaccine unit cost of US\$7 [37], and a study from India and Kenya also reported that introduction of the monovalent rotavirus vaccine would be highly cost effective [39,43], the unit cost per vaccine in India study was US\$7, in the Kenya study the unit cost was between US\$ 9.2 and US\$ 7.4. However none of these studies directly compared the benefit of combining rotavirus vaccine with diarrhoea management,



and all the studies used secondary cost data, either from the WHO-CHOICE project or other vaccination costing studies.

Rotavirus vaccine is expected to provide further societal benefits not captured by our model [44], which only includes the health provider perspective. Even if health services for children in Tanzania are free, the out of pocket expenditure for food, transport, and medicines for diarrhoea are substantial and are estimated to be on average US\$ 5.5 per child admission [45]. In addition to these direct costs, indirect costs associated with productivity loss are likely to be highly relevant. Our model therefore probably underestimates the full societal benefits and, consequently, the cost-effectiveness of rotavirus vaccination. The inclusion of RV5 as a comparator might have enhanced the analysis and hence the results, but we chose to exclude the intervention due to lack of Tanzanian cost data.

Cost estimates for diarrhoea management and rolling out the rotavirus vaccine were collected from only one rural and one urban district. Our findings are therefore not necessarily representative for districts that are different in terms of income levels or other characteristics, or for the whole country. Regional estimates could, however, be useful to inform national scale up. The unit costs for diarrhoea treatment were collected in the absence of an immunization programme. After the rotavirus vaccine roll out, the diarrhoea treatment costs might change because of a possible reduction in the number of OPD visits and IPD days. However, we cannot predict that with certainty from our study. We had no apriori evidence suggesting the degree of economies of scale before vaccine introduction. The cost data may be updated after roll-out to reflect possible impact of vaccine on health care expenditure. Our model can easily be adapted using local and updated data to optimize its local relevance.

The effectiveness data used in this work were retrieved from various meta-analyses lacking direct head to head comparisons between competing interventions. The lack of network meta-analysis may impact on the precision of our study results. Ideally network meta-analysis could have been done to further synthesis the evidence, increase precision of the model results and, hence minimize the potential bias of using effectiveness data from several different sources [46]. However these network meta-analysis are only as good as the trials included in them. In the setting in which this study was conducted, these methods are not well developed and it was beyond the scope of this analysis to perform an independent network meta-analysis. Nevertheless, decisions in health care resource allocation have to be made in this context, even in the absence of precision data and more complex analytical and synthesis methods [47]. For further studies, we

recommend inclusion of network meta-analysis. It would also be useful if well-established bodies such as the Child Health Epidemiology Reference Group (CHERG) and the Cochrane collaboration consider extending the conventional meta-analysis into network meta-analysis to generate evidence for use in low-income settings.

## Conclusions

A combination of rotavirus immunisation and diarrhoea management for Tanzania is likely to be cost-effective when willingness to pay for health exceeds US\$ 112 per DALY. Provisions of RV1 vaccine alone or diarrhoea management alone are both less cost effectiveness alternatives. The roll out of the Rotavirus vaccine as a package with diarrhoea treatment will strengthen the efforts to achieve the child health Millennium Development Goals in Tanzania and should be seen as a high priority intervention for child health improvement.

## Competing interests

GMR, FNN and OFN declare that they have no competing interests. BR received partial funding from GSK for a Norwegian pneumococcus vaccine study in 2010/2011.

## Authors' contributions

GMR collected all the primary cost data and conducted the analyses. All authors contributed in the research design, interpretation of results and writing of the manuscript, and all approved the final version of the manuscript.

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RESEARCH ARTICLE

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# Addressing inequity to achieve the maternal and child health millennium development goals: looking beyond averages

George M Ruhago<sup>1,3\*</sup>, Frida N Ngalesoni<sup>2,3</sup> and Ole F Norheim<sup>3</sup>

## Abstract

**Background:** Inequity in access to and use of child and maternal health interventions is impeding progress towards the maternal and child health Millennium Development Goals. This study explores the potential health gains and equity impact if a set of priority interventions for mothers and under fives were scaled up to reach national universal coverage targets for MDGs in Tanzania.

**Methods:** We used the Lives Saved Tool (LiST) to estimate potential reductions in maternal and child mortality and the number of lives saved across wealth quintiles and between rural and urban settings. High impact maternal and child health interventions were modelled for a five-year scale up, by linking intervention coverage, effectiveness and cause of mortality using data from Tanzania. Concentration curves were drawn and the concentration index estimated to measure the equity impact of the scale up.

**Results:** In the poorest population quintiles in Tanzania, the lives of more than twice as many mothers and under-fives were likely to be saved, compared to the richest quintile. Scaling up coverage to equal levels across quintiles would reduce inequality in maternal and child mortality from a pro rich concentration index of  $-0.11$  (maternal) and  $-0.12$  (children) to a more equitable concentration index of  $-0.03$  and  $-0.03$  respectively. In rural areas, there would likely be an eight times greater reduction in maternal deaths than in urban areas and a five times greater reduction in child deaths than in urban areas.

**Conclusions:** Scaling up priority maternal and child health interventions to equal levels would potentially save far more lives in the poorest populations, and would accelerate equitable progress towards maternal and child health MDGs.

## Background

In September 2000, global leaders gathered at the United Nations assembly and adopted a resolution on the Millennium Development Goals (MDG). Among the main objectives is a two-thirds reduction in child mortality in the under-fives (MDG 4) and a three-quarter reduction in maternal mortality (MDG 5) relative to 1990 rates [1]. Progress towards MDG 4 and 5 is promising with significant acceleration globally [2,3]. However, some developing countries are still lagging behind. In Tanzania,

there have been substantial reductions in maternal and child mortality. Under-fives mortality declined from 141 deaths per 1000 live births in 1990 to 81 in 2010, maternal mortality has dropped from 578 deaths per 100,000 live births in 1990 to 452 in 2010 [3,4]. But these reductions are well short of Tanzania's MDG targets of 54 deaths per 1000 live births and 193 deaths per 100,000 live births for MGD 4 and 5 respectively.

Inequity in access to and use of child and maternal health interventions has been highlighted as hindering progress towards child and maternal health MDGs [5]. A 2010 UNICEF report on progress for children showed that in half the developing countries which had an overall reduction in under-five mortality, inequality in under-five mortality between the poorest and the richest households increased by more than 10 per cent [6]. However the

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disparity in mortality is masked by national average data. In the least developed countries accounting for more than 90 percent of maternal and child mortality globally, there is inequity in coverage of key health interventions, with a country mean coverage gap of 43 among the poorest and wealthiest quintiles of the population [7]. In Tanzania, there is, on average, a 60 percent coverage gap in access to health facilities and skilled birth attendants. The richest populations enjoy 90 percent coverage compared with only 33 percent for the poorest population [8]. Numerous studies have showed that health systems are consistently unjust: likely to provide more and higher quality services to the well-off compared to the poor [9,10]. Health inequities are a consequence of high levels of direct and indirect payment for services, unfair distribution of economic resources, and unequal political and social authority between groups in society [11]. Analysis of equity trends in health outcomes can guide effective and fair service delivery strategies [12]. Therefore it is important to generate evidence about inequity that can inform decision making and priority setting.

Many countries in Sub-Saharan Africa, such as Tanzania, make limited use of scientific evidence to inform policy debate and health care priority setting. Inadequate use of the evidence contributes to inequity in access to and use of child and maternal health interventions and health outcomes. In order to reach MDGs targets, scale up of health interventions is essential. To achieve rapid scale up requires evidence on what works and with what resources. This can guide policy makers and governments in identifying, prioritizing and implementing high impact health interventions [13]. However, targets for the Millennium Development Goals for maternal and child health interventions are set on the basis of national average data. In a recent work, Reidpath et al. [14], used a hypothetical country to show that the use of national average data can conceal inequities in mortality between social and economic groups. Expanding intervention coverage using national average data may not address existing disparities in coverage between socioeconomic groups or geographical locations [15]. In order for the health system to achieve universal coverage, it is important that any scale up addresses the needs of all population groups across geographical locations and socioeconomic status by disaggregating coverage data to reflect distinct groups within society.

Tools such as the Lives Saved Tool (LiST) are useful to policymakers in priority setting. The tool can be used to identify which interventions can be scaled up rapidly and what their impact on mortality may be [16,17]. LiST can also be used to address health distributional impact across household wealth quintiles [18]. Rational, equitable and evidence based priority setting is key to increasing the

coverage of accessible and essential health care interventions. The aim of this paper is to estimate the potential health gains and equity impact if coverage of a set of high impact priority interventions for mothers and under fives were scaled up to the national universal coverage targets for achieving MDGs in Tanzania.

## Methods

### Data sources

We use disaggregated data from Tanzania to reflect mortality and coverage in five wealth quintiles from the poorest to the richest and in rural and urban areas. Baseline coverage and mortality data for this study were extracted from the openly available, 2010 Tanzania Demographic and Health Survey (TDHS) [8]. Permission to conduct research was sought and obtained from the Tanzania National Institute of Medical Research (NIMR). We define universal coverage as 80–90% coverage, acknowledging that the ideal 100% coverage may be hard to reach. For endpoint coverage, we used targets from the 2008 Tanzania National Strategic Plan for reduction of maternal, newborn and child mortality (90% for most targets) [19]. In case national targets were lower than the current TDHS 2010 coverage levels in any of the sub-national or socioeconomic groups, TDHS data were used as endpoint coverage. Table 1 below provides a summary of interventions, coverage estimates and targets.

### Data analysis

We used the Lives Saved Tool (LiST) version 4.47 for modeling. LiST is free, downloadable software and is part of the spectrum policy modeling system developed by the John Hopkins University [20]. The tool was used to model the potential health impact of scaling up priority health interventions on maternal and child mortality for a period of five years. In this study, the baseline year is 2011 and the final year is set at the target for Millennium Development Goals, 2015.

LiST is pre-loaded with country specific average data. To allow for wealth quintile and urban vs. rural analysis, we adjusted the national demographic projection to obtain population estimates for each of the five wealth quintiles as well as urban and rural areas. In other words, we partitioned the whole population into seven “sub-populations” or sub-groups. The national total fertility rate was adjusted by the five wealth quintiles and urban/rural estimates of fertility rates from Tanzanian health and demographic surveys from 1992 to 2010. The adjusted fertility rate was applied from the first year of population to the target year. The proportion of each of the quintiles, urban/rural areas to the total national population was multiplied by the first year population of the national population estimates pre-loaded in LiST to estimate each of the sub-group populations. Migration values were adjusted to zero. The



**Table 1 Intervention coverage (%) for maternal and child health interventions by wealth quintiles and geographical residence used as input in LiST**

Interventions	National	Urban	Rural	Wealth quintiles					Targets
				Poorest	Poor	Middle	Less Poor	Richest	
<b>Pregnancy and child birth care</b>									
Antenatal Care	43.0	54.8	39.1	39.1	39.1	43.0	54.8	54.8	90
Facility based delivery	50.5	83.0	42.0	33.1	36.2	45.8	62.5	89.6	90
Skilled birth attendance	50.5	83.3	42.3	33.0	35.8	47.0	63.3	90.4	90
<b>Diarrhoea management</b>									
Oral Rehydration Salt (ORS)	44.2	44.4	44.0	40.8	42.6	43.3	54.0	38.3	90
<b>Pneumonia management</b>									
Case Management of Pneumonia	42.6	45.6	36.6	34.7	37.0	36.7	39.7	48.7	80
<b>Malaria</b>									
Insecticide Treated Nets (ITN)	63.4	64.9	63.0	56.6	63.9	63.6	66.8	68.0	80
artemisinin-based combination therapy	37.6	33.2	39.1	44.1	36.0	35.6	32.1	36.0	80
<b>Population (%) to national population</b>	100	26	74	19	21.5	21.9	19.7	17.5	

maternal mortality ratio and under-fives mortality rates by SES quintile and urban/rural were updated for the sub-group analysis using current data from TDHS 2010. Default data for cause-specific mortality was used. However, we assumed that the higher/lower than average neonatal, infant and under-five mortality rates in each quintile reported in demographic and health survey were distributed in proportion to the original distribution of cause-specific mortality. The family planning module was updated, the total fertility rate and the unmet need for family planning was adjusted to reflect the sub-group current data. The LiST user manual provides detailed procedures for sub-group modeling [21]. The data on the effectiveness of interventions are default in LiST, updated frequently from comprehensive reviews under the Child Health Epidemiology Reference Group (CHERG) [22].

We entered the baseline coverage for each quintile, urban/rural and national level for a set of high impact priority interventions for maternal health (skilled birth attendance and health facility delivery, as proxy predictors of Basic Emergency Obstetric Care and Comprehensive Emergency Obstetric Care) into LiST. Similarly, coverage data per quintile and urban/rural for child health interventions (oral rehydration salts (ORS) for diarrhoea management, antibiotic for pneumonia treatment, Insecticide Treated Nets (ITN) and artemisinin-based combination therapy (ACTs) for the management of malaria) were entered.

The TDHS 2010, does not report maternal mortality by wealth quintile, so the lowest, midpoint and high estimates were used for quintiles. To account for any possible biases the two lowest quintiles (40%) likely to have higher maternal mortality were assigned with the highest estimates of maternal mortality ratio. The modeling exercises

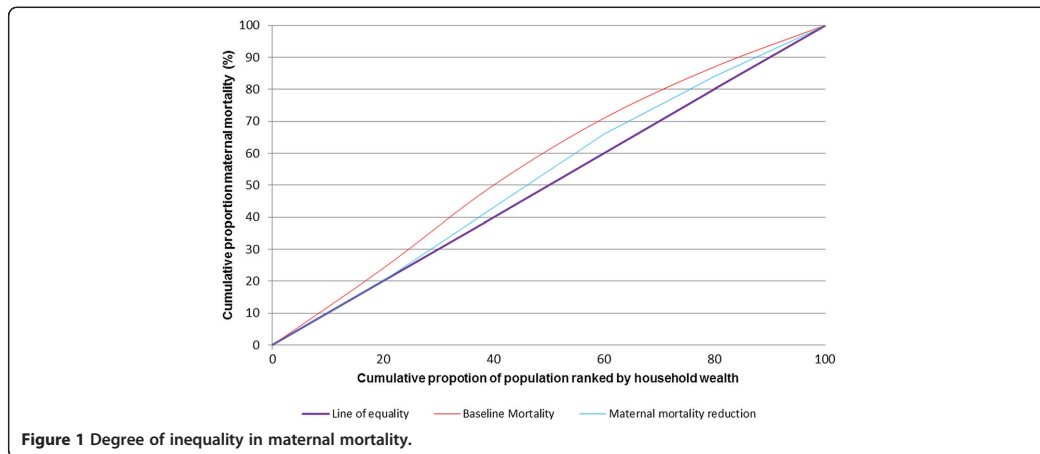
were done by linking intervention coverage, effectiveness and cause of mortality. We observed the expected change of mortality in maternal and under-fives and lives saved over the five-year period. Details on the assumptions built into the LiST module have been well documented elsewhere [23,24].

#### Equity analysis

Concentration curve and concentration index were used to measure the equity impact of the priority intervention scale up. A concentration curve is used to display the distributional impact of wealth related inequity in MMR and U5M, (Figures 1 and 2). The baseline and endpoint mortality measured before and after intervention scale up (maternal or under five mortality) were cumulatively plotted on the y-axis, against the cumulative proportion of (mothers or under-fives) population ranked by their socioeconomic status from lowest to highest on the x axis. When the curve lies on the line of equality, all mothers or under fives, regardless of their socioeconomic status have the same mortality. If it lies above the line of equality, mortality is more prominent amongst the poorest population, indicating a pro-rich distribution. On the other hand if the curve lies below the line of equality, this indicates lower mortality in the poorest population, hence a pro poor distribution. To obtain the magnitude of inequality, we used the concentration index [25]. The measure ranges from -1 to 1, with a zero index indicating no wealth related inequity and a negative index indicating higher maternal or under five mortality among the poor.

#### Results

Table 2 below shows changes in the maternal mortality ratio and deaths averted as a result of the scale

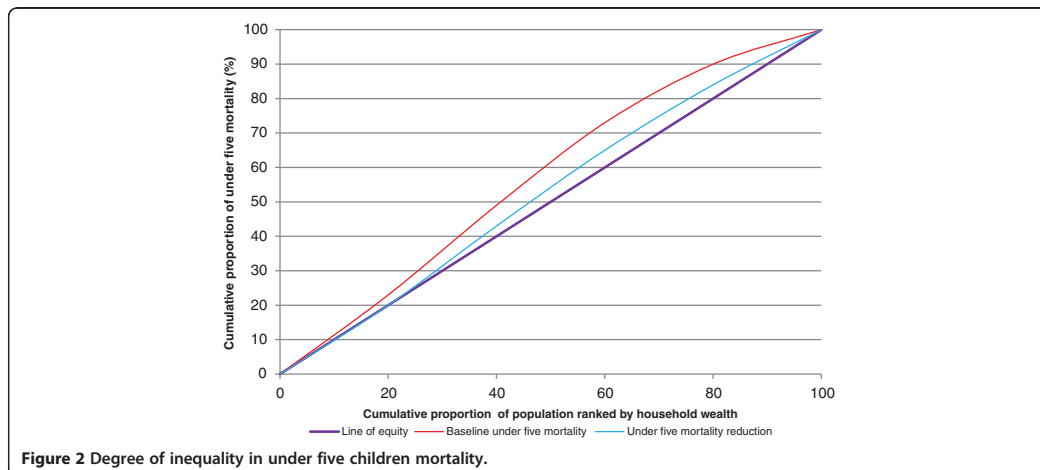


up of high impact priority interventions for maternal health.

The scaling up of interventions by wealth quintile towards equal and universal coverage achieved a significant reduction in maternal mortality: the poorest population benefiting the most, with a reduction in mortality ratio of 286 per 100,000 live births compared with only 156 in the richest quintile. In all, targeting the poorest population saves three times more maternal deaths compared to targeting the richest quintile. That corresponds to a reduction in inequality from a pro rich concentration index of  $-0.11$  to a more equitable concentration index of  $-0.03$ . The pro-poor reduction in mortality is depicted by the concentration curve (Figure 1).

Scaling up rural maternal health interventions to the current coverage level accessible to the urban and richest populations (90%) is likely to avert eight times more maternal deaths, i.e., 4955 deaths averted in rural areas compared to 589 in urban areas.

Table 3 above, describes the outcome of scaling up priority interventions for the three leading causes of mortality in under-fives in Tanzania (diarrhoea, pneumonia and malaria). Increasing coverage levels of health interventions in the poorest under-fives to the same coverage level as the richest quintiles (Table 1) in a period of five years is likely to reduce under-five mortality in the poorest children by 43 per 1000 live births, compared with 31 in the richest population. The poorest population is likely to avert more than twice the number of under-five



**Table 2 Maternal mortality ratio for five quintiles, at baseline (No coverage change), and modeled for endpoint (Coverage change with priority interventions) using LIST**

Population Level	Mortality reduction (per 100,000 live births)			Maternal life saved		
	Baseline (No coverage change) MMR 2011	Endpoint (Coverage change) MMR 2015	Mortality ratio reduction (N)	Baseline (2011)	Endpoint (2015)	Deaths averted by 2015
Richest	353	197	156	925	517	408
Less Poor	353	193	160	1789	761	1028
Poor	454	224	230	2722	1096	1626
Very Poor	556	271	285	2814	1372	1442
Poorest	556	270	286	2568	1255	1213
<b>Conc. index</b>	<b>-0.105</b>		<b>-0.032</b>			
Urban	353	192	45.6	1289	700	589
Rural	556	273	51.0	9740	4785	4955
National	452	248	204	9787	5146	4641
<b>MDG Target</b>			<b>193</b>			

deaths, ie, 18974 in the poorest group compared to 7949 in the richest. The concentration curve (Figure 2), portrays the pro-poor reduction in mortality from baseline concentration index -0.12 to a near perfect equality index at endpoint -0.03.

The scale up of health interventions for the under-fives in rural and urban areas to the same coverage levels of 80 and 90%, over a period of five years, reduce five times more deaths, i.e., 61847 in rural areas compared to 12344 in urban areas.

### Discussion

The results of this study show that using wealth and rural/urban disaggregated intervention coverage in models can guide policy makers on health outcomes and equity impact of scaling up effective interventions in different population groups. The scale up of health intervention coverage to universal levels of 80 to 90% has

potential positive distributional impacts for the worst-off populations and may accelerate equitable achievement of maternal and child Millennium Development Goals. This study has shown that if the wealth and geography-related gap in coverage of a set of high impact priority health interventions is redressed, the under-five mortality rate will be reduced more equitably, may even exceed the target for Millennium Development Goals in Tanzania. Services for the poorest groups would save three times more children compared to the richest groups. The reduction in maternal mortality to the MDG target in Tanzania would be likely to be achieved only by the two richest quintiles, but there would be less inequality in mortality. Rural areas would see a reduction in maternal deaths of eight times that in urban areas, and a reduction in child deaths five times that of urban areas if interventions were scaled-up. At the current coverage, without rapid intervention scale up in Tanzania, MDG 4 is likely

**Table 3 Under Five mortality rates for five population levels, at baseline (No coverage change), modeled for endpoint (Coverage change with priority interventions) using LIST**

Population Level	Mortality reduction (per 1000 live births)			Under five life saved		
	Baseline (No coverage change) U5MR (2011)	Endpoint (coverage change) U5MR (2015)	Mortality reduction (N)	Baseline mortality (2011)	Endpoint mortality (2015)	Deaths averted by 2015
Richest	84	53	31	21534	13585	7949
Less Poor	88	55	33	33599	21105	12494
Poor	91	53	38	41346	25268	16078
Very Poor	92	54	38	44941	26413	18528
Poorest	103	60	43	45803	26829	18974
<b>Conc. Index</b>	<b>-0.119</b>		<b>-0.027</b>			
Urban	94	58	36	32984	20640	12344
Rural	92	54	38	153087	91240	61847
National	81	48	33	164818	100726	64092
<b>MDG Target</b>			<b>54</b>			

to be achieved by 2030 and MDG 5 after 2040 [3]. Therefore, investing in the health of the poorest households and populations in rural areas, and scaling up a few high impact priority interventions could be fundamental to achieving the MDGs. These findings are consistent with those of earlier studies that highlighted the need to address inequity concerns in health care to speed up achievement of the health related MDGs [5,14,26-28].

Addressing inequity is also in line with universal health care policy now being promoted by many UN organizations, public health initiatives, as well as the Tanzanian government [15,29-31]. To succeed in providing universal health coverage, a health system requires qualified human resources, a functioning logistic and supply system, health information systems to assist monitoring and evaluation, good governance and appropriate resource allocation. Shortages of and unequal distribution of human resources for health between urban and rural districts, (the former reported to have more than twice the number of qualified health professionals as the latter), diminishes the chances of reaching the under-served in developing countries such as Tanzania [32,33]. Reinforcing primary care with qualified health workers and strengthening the health system through direct investments in primary health care, with a focus on community health worker in hard to reach areas and in areas with high poverty is important so that universal coverage can reach the poorest populations and reduce inequities in maternal and under-five health outcomes. We believe sub-group analysis in LiST, as demonstrated in this article, is indispensable for making the right decisions at all levels of a health system. Focusing only on average levels of intervention coverage and mortality fails to capture important distributional information which is crucial to strategic decisions for achieving the Millennium Development Goals. A recent study by Carrera, C., et al. has revealed that, health policies addressing geographical and wealth related inequity in child health intervention are cost effective and reduces health care related financial burdens to poor households [34].

Resource allocation in many developing health systems depends on health budget distribution by central government. It is imperative that ways of examining socio-economic disparities in health conditions and service delivery are used to examine population access to health programmes [35], and to inform policy debate and resource allocation. In Tanzania, the health budget, except for salaries, is allocated centrally on the basis of need, where the allocation formula is driven by four main components: population size, which accounts for 70% of the budget; percentage of population below the poverty line; transport needs (district vehicle route) and average under-fives mortality (used as a proxy for burden of disease), which each accounts for 10% [36]. Given the current mortality and coverage rates per quintiles, one

can question whether the current allocation formula sufficiently incorporates concerns for equity. Populated and richer urban districts are likely to receive more funding from central government than rural districts. Incorporating measures of inequity such as the Gini coefficient in the resource allocation formula would explicitly address the health care needs of the worst-off [37].

In interpreting the results of this study, caution should be exercised. Our findings have affirmed that modelling tools such as LiST can be used to generate policy options to aid efficient allocation of limited health care resources. However, even if our modelling on health and equity impact is based on the most recent and best available evidence, our estimates are uncertain and can never be better than the assumptions they rest on. Moreover, we have not estimated the costs of achieving high coverage rates for the worst off quintiles. The estimate of the predicted impact on mortality relies on adherence to the standard quality of medical care. The ambitious scale up in this paper would require substantial investment in the health system and assumes that high quality services could be implemented everywhere and for everyone. This assumption may not hold true. Even if absolute effectiveness is highest in the groups with highest mortality, cost-effectiveness analysis of these interventions for these sub-groups may change the picture. An extended cost-effectiveness analysis is therefore the next logical step from our findings here.

## Conclusions

This study has given an account of how maternal and child health MGDs might be achieved by addressing the health care needs of the worst-off population. The use of scientific evidence to inform policy debates is likely to aid key policy decisions such as training and fair allocation of human resource for health, efficient health financing and expanding community based health care to reach all population. Informed policy choices affecting sub-groups of the population is central to rapid scale up of maternal and child health interventions within a framework of universal health care for all.

## Abbreviations

MDG: Millennium Development Goals; LiST: Life Saved Tool; TDHS: Tanzania Demographic and Health Survey; MMR: Maternal Mortality Ratio (per 100,000 live births); U5MR: Under five mortality rate (per 1000 live births).

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

GMR and OFN: designed the study, acquired the data, analysed and interpreted the results and drafted the manuscript. FNG: contributed in data analysis and manuscript writing. All authors read and approved the final manuscript.

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