Universal health coverage of HIV, TB and malaria interventions in Ethiopia: economic burden, health benefits and financial risk protection

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Thesis for the degree of Philosophiae Doctor (PhD)
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Scientific Environment

The Ph.D. candidate was affiliated to the Department of Global Public Health and Primary Care, Faculty of Medicine, University of Bergen, Bergen, Norway. Professor Kjell Arne Johansson as a principal supervisor and Dr. Mieraf Taddesse Tolla as co-supervisor provided constructive feedback and guidance during the Ph.D. study period. The research was conducted using both primary and secondary data from Ethiopia. The Ph.D. study offers learning opportunities at the Department of Global Health and Population at the Harvard T.H. Chan School of Public Health as a visiting scholar to engage in seminars, courses and organised events that greatly contributes in expanding my educational and research objectives. This research was part of the Disease Control Priorities - Ethiopia project and was funded by the Bill & Melinda Gates Foundation.

Dedication

This paper is dedicated to Selamawit Banjaw Mulatu, my wife. My Ph.D. study is made possible by her unreserved support and ambition. Once more, God bless her.

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Summary

Introduction: Human Immunodeficiency Virus (HIV), Tuberculosis (TB) and malaria remain a major threat to the Ethiopian population. In the past decades, substantial gains have been achieved in reducing morbidity and mortality caused by HIV, TB and malaria diseases. Despite this progress, the coverage of essential health services for these diseases is far below the global targets. The health financing model in Ethiopia heavily relies on out-of-pocket (OOP) spending, which predisposes households to financial hardship. Therefore, high disease burden along with economic barriers have prohibitive consequences on accessing quality health services in the country. In addition, the allocation of scarce healthcare resources needs to be rationed appropriately to improve the health of the population in fair and efficient ways. Furthermore, in Ethiopia, like most low-income countries, apart from the health benefit of interventions to control major communicable diseases, the interventions' importance in greater household economic returns, financial risk protection (FRP) and distributional consequences has not been fully recognised. Hence, evaluation of patient costs and benefits of the scale-up of HIV, TB and malaria interventions through universal public financing on health, equity and FRP domains are essential for priority setting and resource allocation decisions in Ethiopia.

Objectives: This thesis aims to provide evidence on the patient cost, health gains and financial risk protection of HIV, TB and malaria interventions across socio-economic groups in Ethiopia.

Methods: This thesis comprises of three interrelated studies. In Paper-I, a nationwide household survey (for HIV) and a separate cross-sectional survey collected from health facilities selected from Oromia and Afar regions (for TB) was used to estimate the magnitude of patient costs, catastrophic health expenditure (CHE) and its determinants for households affected by these diseases. Patient costs and CHE were used as a primary outcome measure in Paper-I. In Paper-II, an Extended Cost-Effectiveness Analysis (ECEA) method was used to estimate the impact of the universal public finance of selected malaria interventions on health benefits and FRP domains across income groups. Paper-III is based on a national level modelling study to estimate the impact of

the universal public finance of selected TB interventions on mortality and financial risk reduction across income groups over the period 2018-35. The main outcomes were death averted and CHE in Papers II and III, including private expenditure averted and net government costs for Paper-II.

Results: The mean patient cost was $ 78 per year for HIV care and $ 115 per TB episode. Direct patient costs of HIV and TB account for 69% and 46% of the total costs, respectively. The overall incidence of CHE among HIV patients was 20% (43% for the poorest quintile and 4% for the richest quintile) and that of the TB household was 40% (ranging from 58% to 20%, between the poorest and richest income quintiles, respectively). The incidence of CHE is higher in patients with frequent healthcare visits, TB/HIV co-infection, drug-resistant TB and hospitalisation. Inequality in financial risk was present across the different income quintiles, where the lower quintile suffers most. Increasing coverage (by 10%) of artemisinin combination therapy (ACT), long-lasting insecticide-treated bed nets (LLIN), indoor residual spraying (IRS) and malaria vaccines among the population at risk would avert 358, 188, 107, and 38 malaria deaths per year in Ethiopia. The four malaria interventions would avert 440, 220, 125, and 18 cases of CHE, respectively. Similarly, among the four interventions, malaria treatment (ACT) averts approximately $4,277,000 in private expenditure. ACT and LLIN interventions were linked to the largest number of deaths and cases of CHE averted. Those people in the lowest income quintiles have the highest health and FRP benefits. For example, the poorest two quintiles accounted for almost half of the deaths averted, compared to one-third in the richest two quintiles. The government cost of the ACT, LLIN, IRS and malaria vaccine interventions is $ 5.7, 16.5, 32.6, and 5.1 million, respectively.

Implementing active TB case finding from 2018 to 2035 would lead to reductions of 206,000 (27%) and 193,000 (32%) of the expected TB deaths and CHEs, respectively. Similarly, enhancing DOTS for drug-susceptible TB would avert 192,000 (25%) deaths and 93,000 (15%) CHEs; and improvements in MDR-TB care would avert up to 6,300 (1%) and 33,000 (6%) deaths and CHEs, respectively. Both the health and financial risk benefits would be greatest for the poorest two income quintiles.

Conclusion: In Ethiopia, spending on HIV and TB care imposes a major economic burden on households. Healthcare payments for HIV and TB care have adverse impact on equitable access to health services and place the population, especially the poorest, at considerable financial risk. The universal public financing of TB and malaria control interventions saves patient lives and brings higher FRP benefits, particularly among the poorest. Therefore, the Ethiopian Government needs to focus on the universal public finance of health intervention to reduce CHE, foster equity and protect households from the financial risks posed by these diseases.

Keywords: HIV, tuberculosis, malaria, economic burden, equity, catastrophic health expenditures, financial risk protection, universal health coverage, extended cost-effectiveness analysis, Ethiopia.

List of original Papers

This thesis was based on the following three interrelated papers, referred to by Roman numerals in the text:

Paper-I

Financial burden of HIV and TB among patients in Ethiopia: a cross sectional survey. BMJ Open. 2020;10(6):e036892.

Paper-II

Assebe, L.F., Kwete, X.J., Wang, D. et al. Health gains and financial risk protection afforded by public financing of selected malaria interventions in Ethiopia: an extended cost-effectiveness analysis. Malar J 19, 41 (2020). https://doi.org/10.1186/s12936-020-3103-5.

Paper-III

Mortality reduction and financial risk protection benefits of expanded TB control in Ethiopia: findings from a modelling study. (Under review in BMJ Open journal).

Abbreviations

AAU	Addis Ababa University
ACT	Artemisinin-based Combination Therapy
ACEPS	Addis Centre for Ethics and Priority Setting
ART	Antiretroviral Therapy
CEA	Cost Effectiveness Analysis
CHE	Catastrophic Health Expenditure
CFR	Case Fatality Ratio
DALY	Disability Adjusted Life Year
DCEA	Distributional Cost-Effectiveness Analysis
DOTS	Directly Observed Treatment, Short-Course
DS-TB	Drug-Susceptible Tuberculosis
ECEA	Extended Cost-Effectiveness Analysis
EHSP	Essential Health Services Package
FRP	Financial Risk Protection
GDP	Gross Domestic Product
HBP	Health Benefit Package
HCF	Healthcare Financing
HIV	Human Immunodeficiency Virus
HSDP	Health Sector Development Programme
HSTP	Health Sector Transformation Plan
ICER	Incremental Cost-Effectiveness Ratio
IQR	Inter-Quartile Range
IRS	Indoor Residual Spray
LLIN	Long-lasting Insecticidal Nets
LMIC	Low-Income and Middle-Income Countries
MCDA	Multi-Criteria Decision Analysis
MDR-TB	Multi-Drug-Resistant Tuberculosis
OOP	Out-of-Pocket Payments
QALY	Quality-Adjusted Life-Year
ROC	Receiver Operating Characteristic
SD	Standard Deviation
SDG	Sustainable Development Goals
TB	Tuberculosis
TIME	TB Impact Modelling and Estimate
UHC	Universal Health Coverage
UHC-SI	UHC service coverage index
UN	United Nations
UNAIDS	United Nations Programme on HIV/AIDS
US	United States
WHO	World Health Organization

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1. Introduction

Globally, health-financing mechanisms include a mix of public (tax-based systems, health insurance funds and external funds) and private spending (mainly in a form of out of pocket payments), with major variation across countries. Most high-income and middle-income countries depend on the former two financing mechanisms and are important for FRP that ensures individuals receive health services without exposure to financial hardship. In low-income countries, however, such systems are often underdeveloped and many rely heavily on out-of-pocket payments, which can predispose households to an increased risk of financial hardship and health outcome disparities (1-4). Hence, ill-health has substantial adverse economic consequences, and its assessment provides insight into the impact of diseases on household economy (5).

Analysis of the economic burden of disease has grown in the last decades (5), though considerable gaps still remain. Many of the studies focused on describing disease burden at population level with limited disaggregated analysis by disease categories and subgroups. Important policy issues, such as the impact of ill health on medical and non-medical consumptions; on productivity and CHE, are often not addressed in the current literature. Moreover, there is limited evidence of policies that reduce service coverage gaps and mitigate financial risks. Understanding the variation in economic burden across different disease categories and population subgroups is a growing concern for policymakers and researchers, which supports prioritising disease-specific health services according to the economic opportunities they offer (5-7). Infectious diseases such as human immunodeficiency virus (HIV), tuberculosis (TB) and malaria have a greater disease burden and economic impact relative to other chronic diseases and injuries (e.g. renal diseases, cancers and cardiovascular diseases) in low-income countries (6). In such settings, chronic infectious diseases account for the largest population with CHE (21.4 million), followed by renal (3.8 million), cardiovascular (0.4 million) and endocrine (0.3 million) diseases (6).

This thesis examines the magnitude of the household economic consequences of seeking healthcare for HIV and TB complemented by return on investment of the public

financing of TB and malaria interventions in the domains of both health and non-health benefits. Such evidence is of high value for policymakers aiming to identify where the greatest gains can be made in mitigating financial risk in accessing healthcare (8, 9). In addition, the evidence is important in identifying effective policies that support decision-makers in equitably allocating limited healthcare resources (5, 10).

This thesis is structured into eight sections. The first section provides a brief overview and literature summary of key topics that include economic burden of HIV, TB and malaria (section 1.1), universal health coverage (section 1.2), priority setting (section 1.3), health financing (section 1.4), a global overview of communicable diseases (section 1.5), country context covering country profile, healthcare system, and overview of HIV, TB and malaria in Ethiopia (section 1.6). In section two, the general and specific objectives of this research are presented. Section three describes the overall methodology including study setting, methodological and analytical considerations in general, followed by detailed elaboration of the method used specifically in the three sub-studies. In section four, (sections 4.1-4.3), result of Papers I-III are summarised independently. The first result section (Paper-I) presents findings from a cross-sectional survey of HIV and TB patient cost, CHE and determinants. The next result section (Paper-II) presents the health and non-health benefits of the universal public finance of malaria interventions. The third result section (Paper-III) presents expected health and FRP benefits of the public financing of selected TB interventions. Section five starts with a synthesis of the main findings from the three Papers, followed by discussion with relevant literature and a summary of the limitations and strengths. Sections six and seven confer key conclusions and recommendations of the three studies. The final section (section eight) provides the list of references.

1.1 Economic burden of HIV, TB and malaria

HIV, TB and malaria have a profound impact on household earnings and the development of national economy, including a high human physical toll (1, 7, 11, 12). At the household level, the economic effects include the loss of savings and investments due to increased healthcare spending on these diseases. At the population level, these

diseases drain national resources, adversely impacting investments in physical and human capital, which are vital for the economic growth of a country (as measured by, i.e., gross domestic product (GDP)) (5). The economic impact of these diseases on household can be measured using 'direct costs', the expenses related to seeking healthcare and 'indirect costs', the monetary value of lost time due to decreased productivity and health facility visits. Besides direct and indirect costs, these diseases impose intangible costs in the form of pain, suffering, other debilitating symptoms, social isolation, and death, which are less quantified in many studies. In contrast, these diseases are primarily evaluated at population level in terms of their impact on overall economic welfare (5).

HIV, TB and malaria patients face immense pre- and post-diagnosis expenses and financial losses of varying degrees (1), despite substantial global and national investments in high burden countries and sub-Saharan Africa with policy goals of care "free-of-charge" or care at "affordable costs". In several settings, a national "free-of-charge" policy exempts only selected disease-specific interventions, including medicines and diagnostic tests and do not necessarily cover costs related to items, such as healthcare fees for pre-diagnostic services, ancillary medicines, imaging, adverse event monitoring, hospitalisation, and non-medical expenses that patients have to pay for (13-16). An economic modelling analysis in 106 malaria-endemic countries found that 13% of malaria expenditure comes from household payments, which was higher than the OOP spending share of HIV, at 4.7% in 2016 (17, 18). The direct cost of malaria care for patient was found to be within the range of 2-3% of household incomes, compared to 2-6% for indirect payments (1). Likewise, 6.5% of total spending on HIV is OOP (18). However, the TB related OOP payment remains high and accounts for about 19% of the total TB spending in resource-constrained countries (i.e.135 low-income and middle-income countries) (19). A systematic review found an average direct cost of $ 155 per drug-susceptible TB with a two-fold increase of indirect costs (20). However, many economic evaluations of HIV, TB and malaria do not fully capture the indirect patient and household costs in the form of lost income (1, 20). The indirect costs are a non-negligible major contributor to financial hardship for HIV, TB and malaria-affected

households, although the extent differs across diseases (1, 11, 21). For example, persons with HIV and TB have been shown to face higher indirect costs than those with malaria due to longer courses of illness and the need for more repeated healthcare visits (1).

The high direct and indirect care costs can lead to CHE. According to a widely used WHO definition, CHE occurs when healthcare costs exceed 10% to 25% of the annual household income or consumption (22). In several previous studies, total malaria patient cost is less than 10% of household annual income. Households suffer from malaria-related CHE when a family member has complicated malaria requiring hospital admission, recurring episodes, or chronic health effects (e.g. neurological sequelae, anemia and death) (1, 6). Unlike malaria, the total costs of HIV and TB care for many households have been catastrophic, possibly due to the need for long-term care and loss of productive working days due to these diseases (11, 23-25). The adverse health shocks due to spending on healthcare affect the consumption of basic necessities such as food, housing and education (22). Households attempt to smooth out the consumption of non-health goods and services using savings, loans, or asset sales. These coping strategies are not always sufficient to handle the economic shocks associated with these diseases and could potentially lead to the reduction of capital stocks and savings, which increase household vulnerability to future crises. Furthermore, because of high healthcare costs, households may be compelled to reduce the intake of non-health goods and services. In more extreme cases, spending on the care of these diseases may even further impoverish affected households by trapping them in the vicious cycle of ill-health and poverty. In addition, high patient costs can raise a particular concern as they correlate not only with household economic strain but also with deferring health facility visits unless severely ill (26).

The economic consequences of spending on HIV, TB and malaria services are affected by various factors, and quantifying the relative importance of these factors informs the design of effective strategies to reduce financial risks. Unfortunately, few studies have provided adequate detail on factors related to the economic burden of these diseases. Among these factors, the more severe forms of illness require additional care not covered

by the providers or requires hospital admission, resulting in high direct costs and loss of income in countries where people lack insurance (1, 6). A national survey of hospitalised malaria patients in Malawi revealed that each day spent in the hospital was associated with a 2% increase in household costs (27). More generally, households that have endured hospitalisation episodes use multiple coping strategies to protect their consumption compared to those without hospitalisation (7). Another factor influencing the level of household spending on HIV, TB and malaria related care is the baseline socio-economic status, where the poorest spend less on healthcare than the better-off. However, poor households typically pay a relatively higher proportion of their total income and at times can barely afford the services they need (10, 23, 28-30). Thus, the poor tend to face a greater financial burden than the better-off when seeking healthcare. For instance, diseases like TB and malaria trap the poorest in a cycle of sickness and economic hardship. In addition, the poor are more vulnerable to economic shocks caused by prohibitive healthcare costs and are more likely to fall into poverty or continue to sink into poverty while sick. As result, diseases are more likely to worsen income inequality and increase poverty by reducing the per capita income growth for individuals and households (6, 10, 28, 29). Therefore, investing in universal public finance of care for communicable diseases gives the poorest a better chance in life, breaking the spiral of sickness and poverty in order to build a sustainable life and share in the benefits of economic progress.

In endemic countries, the economic impact of HIV, TB and malaria extends from households to affect the general population and national economies as a whole (5). The impact of these diseases takes place through several mechanisms. Where these diseases prevail, the morbidity and mortality burden often falls on children and adults of prime-age (12). Loss of life from these diseases has a profound effect on population size and composition including childbirth. As a result, the diseases have been projected to reduce life expectancy in low-income countries by 1.45 years for HIV, 1.35 years for TB, and 0.96 years for malaria (31). The high mortality rate also results in a marked loss of labour and productivity in the national economy. Furthermore, these diseases can divert government investments in physical and human capital to combat HIV, TB and malaria

in endemic countries, leading to slow growth of GDP over time (17-19). HIV is estimated to reduce national economic growth rates from nil to 2-4% each year (32) and for every 10% rise in reported new TB cases, the country's growth rate is estimated to decrease by 0.2% to 0.4% (33). In malaria-endemic countries, after controlling for other variables, GDP grew by 0.25-1.3% less per year than in countries without malaria (34). In addition to economic growth and demographic changes, the macroeconomic impact of these diseases is expected to accumulate over time and will continue to have long-term consequences in the future. Nonetheless, the existing evidence on the macro-economic impacts of these diseases typically does not take into account the intimate overlaps between the diseases and the loss of social capital or the long-term harm to human capital, as children's intellectual development, health and nutrition go far beyond the period and scope of most macro-economic forecasts (5, 35).

In general, the diseases burden and the financial hardship of infectious disease will continue to put tremendous pressure on the healthcare systems of low-income and middle-income countries (LMICs). This will require policy-makers to improve access to care and ensure FRP alongside broader poverty reduction strategies by formulating measures that accelerate universal health coverage (UHC) as part of a multi-pronged strategy (6).

1.2 Universal health coverage

"Universal health coverage ensures that all people receive the needed health services without being exposed to financial ruin" (2). UHC ensures people accessing ranges of comprehensive services, including prevention, promotion, treatment, rehabilitation and palliative care. Such range of services would progressively expand to reduce the unmet health needs, as no or few countries can afford to instantly finance a full set of services to all people (36, 37). UHC also requires countries to build their health systems in a way that guarantees equity, FRP and better health. The lack of physical access, poorly equipped health facilities and inadequate quality of care are among the main barriers to accessing essential health services in LMICs. Furthermore, socioeconomic factors have a major effect on access to healthcare and, subsequently, on health outcomes. Hence,

UHC encompasses different health system components, including service delivery, financing policy, information system, infrastructure, health workforce, drug supply management, and governance (2).

The path to UHC is not straightforward; in every country, some systems are in place and each country needs to build on the existing systems to progress towards UHC (2, 36). However, to achieve the goal of UHC, each country needs to step forward in at least three distinct aspects : (a) the proportion of people covered by pooled funds (b) the range of available services (expands over time) through UHC policies and (c) the cost required from pooled funds to deliver health services (Figure 1) (2). As countries move along these dimensions, they will need to make critical policy choices in terms of maximisation of benefits, fairness and other concerns (36). These decisions involve trading among the fraction of the population reached, the range and types of services included, and the cost covered by the pooled funds in order to achieve 100% coverage in each dimension.

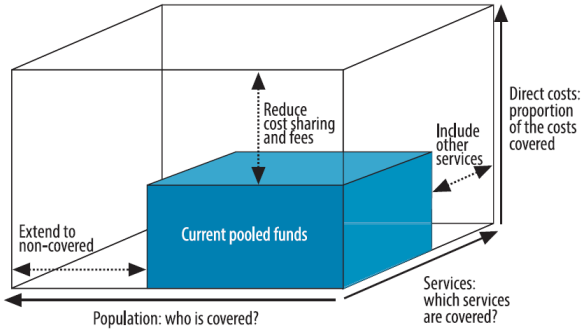


Figure 1: Three-dimensional framework and critical choices in the path towards UHC. Source: The World Health Report 2010.

UHC is among the priorities of the Sustainable Development Goal (SDG) and is the base of SDG 3. SDG 3.8 has two key indicators to track progress towards UHC, namely the essential health services coverage (SDG 3.8.1 indicator) and the percentage of individuals or households with CHE (SDG 3.8.2 indicator). Both indicators are intended to capture effective coverage and FRP dimension of progress towards UHC (38). In particular, the service and cost coverage dimension are related to the UHC objectives of

effective coverage and FRP, respectively, while the population axis is related to both. Monitoring financial risks along with access to essential services are very important on the path to UHC. In particular, a low incidence of CHE means that either people are successfully shielded from financial hardship or are not able to access health services at all (i.e. low service coverage). Conversely, even if the service is made available or delivered as a result of reforms, it should also be accessible and affordable to all in need of care. Hence, a combined analysis of both indicators would provide a more precise specification of UHC (4).

The UHC Service Coverage Index (SCI) is a summary index derived from the coverage of 14 tracer indicators and is used to track country progress towards SDG 3.8.1. In 2017, close to half of the world's population is covered by essential health services. This achievement is mainly attributed to the performance of the 14 tracer indicators, with the greatest contribution to this coverage coming from HIV, TB and malaria services. Nevertheless, the rate of progress is still slow for many services and unevenly distributed across socio-economic groups requiring the coverage of essential health services to double in order to meet UHC's SDG target by 2030. Globally, CHE has been increasingly rising and FRP is declining over time as tracked by indicator 3.8.2. Between 2000 and 2015, the proportion of the world's population with OOP exceeding 10% of household income increased from 9.4% to 12.7% (926.6 million people) and globally an estimated 1.2% (89.7 million people) are pushed into extreme poverty. Policy implications of UHC progress differ across countries as there are large variations in terms of service coverage and FRP outcomes that require comprehensive reform of both service delivery and health financing systems for low-income countries; and enhancing efficiency, quality and equity gains for high-income and upper-middle-income countries (4).

The Ethiopian Government has continued to develop important strategies to move towards UHC. The latest national revision of the essential health services package (EHSP) is one of these critical endeavours. The first EHSP was set up in 2005 and revised in 2019. The EHSP is not only aimed at ensuring equitable access to high-quality healthcare through the provision of affordable, high-priority interventions, but it also acts

as a guiding framework to attain UHC for essential health services in the country. The EHSP proposes the types of services offered under the current health service delivery system that should be available to all Ethiopians, regardless of income, gender and place of residence. The EHSP is defined primarily based on disease burden in Ethiopia, in addition to six other relevant criteria (i.e. cost-effectiveness, budget impact, equity, public and political acceptability, and FRP). The prevention and control of communicable diseases was one of the main components of Ethiopia's EHSP and was deemed a high priority based on the above criteria. Thus, the effective implementation of the EHSP would strengthen access to affordable care and protection of financial risks related to HIV, TB and malaria services in the country from now on and in the future (39). For the realisation of the EHSP, a sustainable system of health financing through effective and efficient payment modalities is also necessary. In Ethiopia, the EHSP financing is organised in three different categories from the patient/client perspective and the financing arrangements are assigned on the basis of the priority level of intervention. The first category is that high-priority health services are offered with universal public finance (e.g. immunisation, malaria, family planning, childbirth services and TB at primary health care facilities). The second category includes medium-priority services that are financed based on cost-sharing mechanisms where direct OOP payments fund a proportion of the provider costs of these interventions. The third category is non-essential health services provided on a full cost-recovery basis and such services were mostly provided in private healthcare settings. However, from the perspective of providers, a clear and sustainable funding system must be in place for all programmes that would allow health facilities to provide quality health services without financial limitations (39).

The implementation of UHC policies in many developing countries represents an important opportunity to address or combat HIV, TB and malaria diseases. UHC ensures that all essential services for HIV, TB and malaria are accessible based on the needs of individuals, without exposing them to financial hardship, thus mitigating the transmission of these diseases. Furthermore, UHC has the potential to accelerate progress towards addressing certain communities that are unreached and marginalised. In essence,

early access to high-quality HIV, TB and malaria services under UHC is essentially more cost-effective than providing low-quality and delayed diagnosis and care. For instance, every dollar spent on treating people with HIV, TB and malaria before complications or drug resistance occur are estimated to give $ 28, $ 43 and $ 36, respectively, in return (40). Even if UHC offers an opportunity to extend service coverage for communicable diseases, scarce healthcare resources and increasing population demands push countries into priority setting and a discussion about which services should be included in the Health Benefits Package (HBP) (36).

The decision to select the best alternatives and the appropriate mix of interventions to be covered by UHC schemes in the light of limited healthcare resources requires appropriate and fair priority-setting criteria (for example, priority for services that provide good value for money, priority for the worse-off and priority for services providing FRP) that are decided through deliberative and consultative processes (36).

1.3 Priority setting in health care

Priority setting is an inevitable continuous exercise required at all levels (global, national, and local) of the health system and addresses the populations' most critical health needs by choosing the appropriate health policy among different alternatives. However, priority setting is a difficult and inherently political process that involves public debate and negotiation among multiple stakeholders, each with different views, values and interests as to who will or will not benefit from public resources and when. Effective priority setting addresses these varying views and interests through evidence and a transparent approach to determine health policies and services that are most appropriate. Priority setting also needs strong political commitment and financial support to accomplish its goals (41).

Priority setting has three main components, namely fact, values and processes (42). Facts are mainly empirical evidence on the effectiveness of the intervention to be prioritised. Values are grounded in ethical principles and criteria (i.e. utilitarianism, egalitarianism and prioritarianism) on which to base the priority decisions. The processes are mainly

related to employing a framework for a rational prioritization process. A systematic review indicated that a variety of processes exist in well-functioning health systems. Accountability for reasonableness is an ethical framework that focuses on the reasonableness of decision-making process, although the approach is not straightforward and replicable. Another multi-criteria decision analysis (MCDA) approach is a method that simultaneously assesses health policies or interventions in the health sector against various criteria. This exploratory analysis defines a range of relevant criteria, including both medical and non-medical, and weigh their relative importance in guiding priority setting. The method has been widely used in other areas, such as agriculture, energy, etc., and experience in other sectors has contributed to the acceptance of this approach for public health decision-making. For example, the MCDA is used to assist policy decisions in the implementation of a lung health programme in Nepal, and the programme is considered one of the priorities based on various relevant criteria (43). Programme budgeting and marginal analysis is another method of priority setting process that evaluates the costs and benefits of planned investment or disinvestment, using a transparent, replicable method and formal participation of stakeholders (panel of experts). The exercise has been applied for effective allocation of healthcare resources in high-income countries (44). This approach was used in North Wales UK to optimise resource allocation alternatives for respiratory care pathways and identified investment opportunities such as the management of pharmaceutical wastes and pulmonary rehabilitation and disinvestment areas including mucolytic and prescription of high-cost antibiotics (45). The priority setting processes mentioned here are not exhaustive and others are also available (e.g. marginal budgeting for bottlenecks) but lack a framework for decision-making processes, or are not routinely used. A review from 2012 concluded that there is no generalisable priority setting process, and each of these approaches should be evaluated and adapted to the need and context of each country (44). A list of criteria or principles representing the three components (facts, value and process) provides an appropriate basis for priority setting decisions (42, 46). In particular, the criteria are selected in a way that addresses the 'values' or agreed on principles on which

the decisions are based and then gathers clinical facts about the possible effects of interventions in terms of 'values' that are supported by fair processes (42).

Priority setting decisions can also be categorised based on the level of decisions addressed by the process. The macro level refers to the global/national level, where resource allocation decisions have been made. At the meso-level, this relates to the regional/district level, where decisions have been made on the healthcare programme. At the micro-level, decisions about patient interactions were made in health facilities (47). Each one of these levels affects one another. Macro-level decisions on health service resources, for example, affect micro/patient-level decisions (42).

Priority-setting decisions also consider the transparency of the process and are classified as explicit and implicit. Explicit was based on clear and well-defined criteria, participatory approach, and fair and accountable processes that are more important during priority setting as they prevent the unfair, uninformed and non-functional processes. Implicit (ad hoc) is the opposite, which lacks a transparent discussion on the criteria and joint evaluation of the evidence during priority setting. When priorities are implicitly set they are more prone to pressures and individual interests, and many other factors play role that may not be in the interest of the population. Priority setting is often implicit (ad hoc) in LMICs, where political pressure accompanied by lack of evidence and funding play a more important role than the process evaluation (44, 48). Consequently, careful consideration of the systems and other contextual factors are very important in LMICs, in addition to an explicit priority setting. In general, when people are informed of the decision-making process and its outcome and the consequences, priority setting is preferable and acceptable, though may sometimes appear too complex or technically challenging to be fully explicit (41, 42).

Explicit priority setting can be made using a set of well-defined criteria and the process may yield evidence-based policies or offer transparent rationale for including or excluding interventions. Such criteria can emanate from the health system goal of improving population health and fair distribution of health benefits (2, 36). Typically, explicit criteria for priority setting may contain elements of disease burden, health

benefits, cost-effectiveness, acceptability and equity (41, 49) (Table 1). The choice of the criteria and weight assigned to each of them will differ according to people preferences. For example, in the selection of high priority services for the progressive realisation of UHC, at least three criteria should be considered, including priority for cost-effectiveness, worse-off, and FRP (36).

Table 1: Example of criteria used in priority setting in various low-income and middle income countries.

Category	Number of studies included	Criteria for Priority setting
Overall	42	Cost-effectiveness (52%), health benefits (45%), and equity (43%)
Country region by income		
• Low-income	14	Cost-effectiveness, health benefits, severity of disease (50% each); equity (43%)
• Lower middle-income	10	Cost-effectiveness, health benefits (44% each); legal and regulatory framework, political considerations
• Upper middle-income	18	Cost-effectiveness; equity; health benefits (47% each)
Level of priority setting decision		
• National(macro)	35	Cost-effectiveness (54%), health benefits (51%), and equity (40%)
• District(meso)	4	Cost of care, cost-effectiveness, feasibility of implementation (50% each)
• Hospital(micro)	3	Equity (67%)
Priority setting approaches		
• Accountability for reasonableness	7	Fairness/ethics, equity (50% each); burden of disease, severity of disease, health benefits (33% each)
• Health technology assessment	2	Health benefits (100%); cost-effectiveness, provider acceptability, legal and regulatory framework for implementation (66.7% each)
• MCDA	8	Health benefits (100%); cost-effectiveness, the severity of disease, equity, legal and regulatory framework (50% each)

Source : adapted from a systematic review by Kaur et al (49).

In summary, priority setting in the three dimensions of UHC may help to identify interventions that meet the health needs of the whole population in general, and vulnerable groups in particular, without causing medical impoverishment (41). In

working towards UHC, countries need to determine which package of interventions to expand first, how to extend the range of services to disadvantaged groups like poor and rural communities and how to switch from OOP to pre-payment mechanisms. Therefore, the following section focuses on three important criteria that are considered acceptable by all theories of distributive justice (i.e. cost-effectiveness, priority for the worse-off and priority for service offering FRP) (50).

1.3.1 Priority to services providing good value for money

Cost-effectiveness analysis (CEA) assesses the opportunity cost of investing in alternative health interventions by comparing costs and health gains. It aids healthcare decision-making by identifying interventions that maximise population health for a given level of resources (51). Spending the scarce resources available for interventions that provide very little health benefit would result in lost opportunities to avert more deaths and prevent serious complications from these diseases/conditions. Thus, cost-effectiveness analysis provides valuable insights into the economic attractiveness, where the intervention with the lowest value for money is placed at the bottom (52).

To illustrate the opportunity cost involved in deciding between interventions, the CEA approach accounts for both the effect and cost of interventions (51). The effect or outcome is mainly measured in natural units, ranging from intermediate outcomes such as blood pressure reduction to more distal endpoints such as deaths averted, and life-year gained, etc. (51). Often, the health effects are difficult to describe in a single effectiveness unit and, for example, treatment intervention apart from affecting survival can also affect the health status which is often not captured in the above effectiveness measures. Therefore, one of the main challenges of the cost-effectiveness approach is to create a single outcome measure that summarises the effect on both the quality and quantity of life or quantifies the disease burden. A summary measure of health status, like quality-adjusted life-year (QALY), incorporates preferences for both the quantity of life lived and quality of life into a single metric, while disability-adjusted life year (DALY) represents a weighted combination of the year lived with the diseases and lives lost as a result of premature deaths. DALYs may therefore be considered as an inverse of QALYs

that have been standardised for comparative use (53). The choice of outcome measure largely depends on the type of intervention being evaluated or the study context. However, the use of distal health outcomes is commonly recommended as a basis for cost-effectiveness analysis to allow comparison with various alternatives. Another component of the CEA is to identify, measure and valuate resources at their "opportunity cost". Both variable costs and the allocated share of fixed costs are included in the total cost, but researchers can limit the scope and concentrate only on variable costs. The CEA uses estimates of both the healthcare costs and effects for computing the net or incremental cost and effects of mutually exclusive alternatives and presents this result in the form of cost-effectiveness ratio (i.e. the cost per unit of health effect or cost per DALY averted). When the cost-effectiveness ratio is estimated relative to the next best alternatives are referred to as incremental cost-effectiveness ratio, while estimation from do-nothing option is described as average cost-effectiveness ratio. The cost-effectiveness ratio mainly depends on the perspective of the analysis, the definition of interventions and the scope of costs (51, 54).

The CEA outcome, i.e. the average or incremental cost-effectiveness ratio (ICER) needs to be complemented by decision rules to determine the worthiness of the intervention for further consideration. Numerous approaches have been suggested to decide on best buys; the first approach is to finance interventions starting with the most cost-effective (i.e. the goal is to maximise population health under a fixed healthcare budget) and moving down a rank-ordered list (i.e. league table) until the budget cap is reached. This approach is affected by the availability of cost-effective data and omits other factors influencing decision-making. The second approach is to use the cost-effectiveness estimates of a benchmark intervention that has already been adopted in the relevant country as a threshold to represent good value for money. Although such an approach may have greater local relevance, the use of a single benchmark intervention does not answer the pressing issue of whether there could be other alternatives that have a greater cost-effectiveness ratio than benchmark intervention. This may be mitigated by using aggregate data on willingness to pay for a unit of health benefit from a wide range of countries (55). The third approach is setting a threshold based on national per capita

income. Generally, costs less than one and three times the national annual GDP per capita per DALY averted are considered highly cost-effective and cost-effective, respectively. The use of GDP-based per capita thresholds is of concern because it lacks empirical and theoretical foundation and ignores budget or affordability issues (55). Indeed, experts argue that the benchmark for placing importance on health needs must be firmly situated within the notion of resource constraints and the relevant context (55, 56). The proposed benchmarks include 1-51% times GDP per capita for both low-income and middle-income countries and 18-71% times GDP per capita for middle- and high-income countries (57). Ideally, context-specific thresholds focused on the opportunity cost of financing healthcare better guide resource allocation decisions and promote population health (56, 57).

In practice, CEA is data-intensive and challenging in LMICs and few studies are available for LMIC settings. CEA evidence for resource constrained settings are made available from the Disease Control Priorities Project, the World Health Organization (WHO)-choosing Interventions that are Cost-Effective and Tuft University CEA database (58-60). However, the comparison of the CEA ratio estimates or the applicability of the result to other settings depends on the contextual factors, in particular, local epidemiological conditions, the existing coverages, potential risks and the health system performance which are crucial in making use of cost-effectiveness analysis (52).

In summary, CEA is highly critical in providing valuable information to decision-makers about choosing which interventions to prioritise when the concern is to increase population health at a low cost. Interventions with low ICER (relatively inexpensive) can be financed by re-allocating ineffective or less cost-effective interventions. If it is not feasible to shift funds from such interventions, future budgetary increases to the sector could be directed to finance these interventions in order to achieve more (54). However, in combination with other relevant criteria that include affordability, budget impact, fairness and feasibility, CEA effectively guides priority setting decisions for the health sector (41). For example, malaria and TB interventions have similar costs per death, but the higher care costs and loss of income associated with TB would entail much greater

FRP benefits from the latter and probably better investment until resources are available for both (61). At a given budget, CEA identifies interventions that provide the greatest health benefit though does not explicitly address the distribution of health and FRP benefits across subgroups that were important in priority setting, which will be the focus of the following section.

1.3.2 Priority to services benefiting the worse-off

In a perfect health system, available healthcare should be equitably distributed based on needs, without any other barriers to access (62). However, health inequities related to access, utilisation and health outcomes are evident and largely determined by economic, social and individual factors such as sex, age, place of residence, education, income, and ethnicity, etc. Worse-off can be defined mainly in two ways. Firstly, individuals who are at a lower absolute level in terms of health needs or severity and benefiting this group matters more (36). Second, the worse-off also refers to the most disadvantaged groups in areas other than health, which includes the poor, the marginalised communities, rural residents and migrant workers, etc. (36). As a consequence, disadvantaged groups often bear the greatest burden of health problems and receive the least care available where they are most in need — the inverse care law (63). Principles of fairness motivate, one way or another, priority to services benefiting the worse-off and, as a consequence, promote equality in health and access to care (36, 54). Nevertheless, worse-off populations may be hard to reach and require innovative strategies that may be costly.

Often, cost-effectiveness and priority to worse-off are not in conflict. However, in some cases, decisions may involve trade-offs between maximising aggregate benefit and reducing health inequity. Such trade-offs may occur, for example, in the delivery of services that improve the overall well-being of the community but involve additional costs to improve access to vulnerable populations due to added infrastructure requirements, lack of trained human resources, or other utilisation barriers (64). These conflicting concerns require an explicit method for weighing trade-offs between improving total population health and distribution of benefit across population groups.

Distributional Cost-Effectiveness Analysis (DCEA) is a methodological framework that expands the CEA model and incorporates both the objective of maximising the overall health and reducing health inequity through healthcare programmes. DCEAs help to quantitatively examine the distributional impact of healthcare interventions and whether more or less equity may be achieved. DCEA methods can assess equity impact with inequality indexes such as the Gini index or concentration index (equity impact analysis) and quantify trade-offs between total health and health equity (i.e. equity trade-off analysis). The equity trade-off analysis uses indexes including the Atkinson or Wagstaff achievement index, where the implications of a broad range of inequality preferences on a policy decision are explored (65, 66). Such type of analysis can answer how strong the preferences for equity need to be in order to change which policy option is deemed most favourable. The equity trade-off analysis was divided into two; an equity constraint analysis and equity weighting analysis. An equity constraint analysis counts the cost of choosing a fairer but less cost-effective policy. A direct equity weighting analysis is a type of multi-criteria decision analysis that adjusts costs and/or effects to the extent to which distributive concerns such as severity, poverty or gender inequality are affected (64, 66).

Finally, when selecting which services to expand first, many recommend starting with cost-effectiveness evaluations of the interventions of interest, and then continue with the assessment of other relevant criteria (36). This is what very often happens in practice, at least.

1.3.3 Priority to services that offer greater financial risk protection

FRP ensures that people receive the needed health services without financial ruin (2). FRP offers an insight into the influence of health systems on the non-health side of people's lives (67). It is more important in countries where prepaid systems are not relatively strong and people have incurred high OOP costs (68).

Out-of-pocket payments often lead to severe financial strain on families and can lead to CHE and impoverishment (26). Healthcare expenditures above 10% of total annual

household expenditure or 40% of total annual non-food expenditure is a widely used definition of CHE. Impoverishing expenditure is related to healthcare payments causing households to fall below a fixed level of absolute poverty (22, 26). Both indices are widely used measures of the financial risk associated with healthcare and represent the failure of the system to shield people from the economic impacts of accessing health services (6). Even though the latter is not, per se, part of the UHC SDG indicators, medical impoverishment explicitly ties UHC to the first SDG goal of "ending poverty in all its forms everywhere" (69).

FRP can be used as a relevant criterion for the selection of services for HBP and is affected by the choices of services (36). For example, the inclusion of high-cost services in the HBP or the lowest-cost but frequently used services provides an efficient way to purchase FRP. Verguet and colleagues suggest methods to determine the value of a given intervention beyond health benefits that involve FRP benefits (68).

In light of these concerns, extended cost-effectiveness analysis (ECEA) is a method that "was developed by Disease Control Priorities, 3rd edition" to assess FRP benefits along with health outcomes and distributional impacts resulting from health policies. ECEA is a methodological extension of CEA that independently quantifies the relative importance of a health policy instrument for different objectives that enable policymakers to consider multiple criteria during priority setting or formulation of HBP. This methodological framework is particularly relevant in LMICs, where prevention of CHE is a key concern alongside the maximisation of population health. More broadly, the use of ECEA techniques quantitatively estimates the impact of health policies on various dimensions that enable comparisons with other disciplines, such as agriculture, education, and transport.

One of the main policy instruments is universal public finance, which is "Government financing of health intervention irrespective of who is receiving it" (70). The public-financing policies can improve access to healthcare by implementing effective and efficient interventions that otherwise would not be available, thereby providing health impact (i.e. health benefit). As services are publicly funded, there is no fee at the point

of use that entails financial gain for the user in terms of cost-saving (i.e. crowding out OOP). Finally, public financing offers insurance against financial risks and prevents CHE (i.e. a major benefit in countries with less efficient insurance systems). The ECEA method quantifies intervention policy impact in three health system outcomes: 1) health gain, 2) private expenditure averted and 3) FRP; all disaggregated by relevant subgroups in a given policy context (e.g., income quintile, gender, geographic, disadvantaged groups). Universal public finance requires additional investments in rural and underserved areas, such as training, facilities, infrastructure improvements, etc., and expanding health services. Lack of such investments can limit the coverage that universal public finance can achieve. The ECEA method helps to identify interventions that are cost-effective in reducing mortality alongside FRP benefits, or narrowing the equity gap between the poor and rich. The outcomes in the three domains, however, might yield contradictory findings; the first category attempts to maximise health by increasing the number of deaths or DALYs averted, while the second assesses interventions based on the number of catastrophic/poverty cases averted or the decrease in the health equity gap. Currently, ECEA does not provide a method to aggregate or rank these diverse benefits. However, the right balance usually requires a decision maker to account for health gains, FRP and equity benefit trade-offs and weighing each outcome depending on the objective of HBP of the country (the detailed methodological aspect of ECEA will be discussed in section 3.2.4) (68, 70).

In summary, protection from financial risks has emerged as an important policy objective for national health sector programmes in many countries. The healthcare financing arrangement greatly matters for financial protection and countries differ considerably in their FRP coverage. In general, countries that rely on the public financing of the health system provide better protection against financial risk through diverting OOP payments into pooled and compulsory prepayment schemes (9, 36, 71).

1.4 Health financing

Health financing plays a vital role in health systems to maintain and enhance human welfare. Health financing refers to the "function of a health system concerned with the

mobilisation, accumulation and allocation of money to cover the health needs of the people, individually and collectively, in the health system…the purpose of health financing is to make funding available, as well as to set the right financial incentives to providers, to ensure that all individuals have access to effective public health and personal healthcare" (2).

The health financing system often focuses on three inter-related core functions, which include (i) revenue-collection: mobilising sufficient resources from a combination of domestic and external sources (i.e. prepayment schemes, government taxes, OOP payments, and donor funds) for the health system; (ii) risk-pooling: the accumulation and redistribution of prepaid financial resources to provide FRP across all scheme members, and pooled funds can be derived from tax and health insurance (i.e. compulsory or voluntary prepaid insurance schemes) contributions and come from a mix of sources in most countries; (iii) purchasing/provision of services: allocation of resources to health service providers so that appropriate and efficient services are available to the population (72). Countries' HBP must be organised under the three core functions of the health financing system to realise the defined benefits in practice.

Notably, countries' health financing models are a hybrid of public (e.g. tax-based, health insurance funds and external aid) and private mechanisms (e.g. private spending mostly paid OOP) and the need for coordination between these funding sources is crucial for achieving UHC (3, 73). More importantly, relying more on universal public finance (e.g. financing from general taxes and obligatory health insurance) plays an important role towards UHC. Universal public finance ensures universal coverage of publicly funded priority interventions and decreases the payment of healthcare at point of service use. In addition, universal public financing would enhances equity by cross-subsidisation from the better-off to the worse-off and from the well to the ill. Most countries have recognised the importance of public finance, and health-financing reform is being pursued in the direction of prepaid sources through general taxation, health insurance, or a mix of approaches. However, the progress of countries differs, where public finance is dominant in high-income countries and private spending is common in LMICs (73). Effective

health financing reforms towards public finance (i.e. tax and health insurance) are important for LMICs to promote equitable use of needed services, quality in service delivery and cost efficiency by making the system more accountable and transparent (9, 73). Therefore, the reforms have a direct impact on the progress of countries towards UHC goals by reducing unmet service needs, improving health and FRP (37).

The Government of Ethiopia has been implementing a healthcare financing (HCF) strategy over the past two decades. As part of this strategy, the government has introduced a wide range of healthcare financing reforms in the areas of resource mobilisation, risk pooling and strategic purchasing for the health system to ensure long-term financial sustainability (74). Among the reforms introduced are revenue retention and use at health facility level, a fee-waiver system for the poor, revision of user fees, standardised exemption of services, provision of service through private wings, outsourcing non-clinical services, implementation of health insurance, and promoting health facility autonomy through the introduction of a governance system (75). As a consequence, the period has been characterised by a huge expansion in health investment, primary healthcare infrastructure, and human resources development (75).

The implementation of the HCF policy has led to a rise in the country's overall health spending, with increased total health expenditure (all financing sources) from $ 230 million in 1995/96 to $ 3.1 billion in 2016/17 (i.e. 4.2% as a share of GDP) (76). Similarly, the per capita spending on health increased from $ 4.1 to $ 33.2 during the same period (76). Nevertheless, this amount is far below the WHO's recommended $ 112 per person need to avail essential healthcare services in low-income countries (77). The major sources of health system financing in the country are donor grants, OOP spending and domestic government expenditure which accounted for 35%, 31%, and 32% respectively. The share of OOP spending out of the total health expenditure has dropped from 53% in 1995/96 to 31% in 2016/17. Approximately 1% of OOP household spending was pooled by community-based health insurance (76). While attempts have been made to decrease the impact of OOPs overtime, the amount of change was too small and far above 15-20% to protect households from catastrophic and impoverishing

expenditures (2). In general, health systems requiring lower OOP healthcare costs offer greater protection against CHE. In particular, this would be achieved by reducing OOP and relying more on prepayment schemes backed by high-quality health services (2). In terms of financing health systems, the country still faces various challenges, such as reliance on private spending, external support and underdeveloped prepayment schemes, which indicate that there is an ongoing need to expand equitable and effective prepayment mechanisms and strengthen the shift to domestic financing in the country (76, 78).

Moreover, the prevention and control of these diseases have been largely supported by external funding, such as the Global Fund, which covers a resource-intensive portion of the programme, in particular for drugs and reagents. The global economic downturn and flattening of international funding for HIV, TB and malaria threaten the sustainable financing of the diseases. If the momentum of financial aid for HIV, TB and malaria is declined or discontinued, these services will be difficult to continue unless substituted by domestic sources in the future (79). Generally, countries heavily dependent on aid have weaker health systems compared to those that consider aid as complementary to government health expenditure. Therefore, increasing government health spending from domestic sources is vital for improving the health in low-income countries, including Ethiopia. The country remains committed to pursuing initiatives aimed at improving and developing more sustainable health financing through the gradual replacement of external to domestic sources. Initiatives intended to increase health financing include i) scale-up of health insurance schemes ii) improve domestic health financing mechanisms (e.g. innovative financing) iii) health facility revenue generation and effective utilisation iv) standardised healthcare fee etc. Besides domestic financing mechanisms, improving efficiency and effectiveness in the health sector is key to providing more health with as little resources as possible (78).

1.5 Global overview of HIV, TB and Malaria

HIV, TB and malaria remain major threats to global health (12, 80). In 2018, an estimated 37.9 million prevalent HIV cases were reported worldwide, with 1.7 million new HIV

infections (81). Similarly, 10.4 million new cases of TB were reported and 8.9% were co-infected with HIV (82). Malaria is a constant threat in many countries, with an estimated 228 million cases occurring worldwide (83). In 2016, approximately 3 million people died of these diseases (81-83). The bulk (i.e. two-thirds) of morbidity and mortality (i.e. 75%-91%) linked to HIV and malaria occurred in sub-Saharan Africa (84). TB, however, is more widespread, where 84% of the burden is contributed by the 30 high-burden countries, mainly from Southeast Asia and Africa (12, 82).

The concerted efforts and commitment in improving access to antiretroviral therapy, standardised treatment of TB and artemisinin-based combination therapies (ACT) and mass bed net distributions have resulted in millions of lives saved over the past two decades (12). In the years between 2000 and 2017, new HIV, TB and malaria infections fell by 49%, 21% and 37%, respectively (31), with estimated 60 million lives saved between 2000-2013 (12, 85-88). Hence, the HIV epidemic is no longer necessarily a life sentence, millions of TB deaths were averted and shrinking the malaria map has become a realistic goal for many countries (89, 90).

Despite the major progress made in addressing the three epidemics, global progress is precariously at risk. About half of HIV positive people are unaware of their status, one-third of TB cases have been undetected and half of the world's population lives in malaria at risk areas (82, 83, 85, 91). During the early years of the sustainable development goal (SDG) era, a huge gap is observed between reality and the vision of sustainable health (83, 92). Recently, the trend towards reducing new adult HIV infections has largely stalled worldwide. HIV infection remains a major concern among key populations including injecting drug users, transgender people, migrants, mobile populations, inmates, sex workers and men having sex with men (93). The overall TB incidence reduction between 2015 and 2018, at the current pace of progress, was only 6.3%, reflecting a 20% deficit relative to the End TB Strategy milestone by 2020 or later (92). In 2018, a global 20% difference in malaria incident cases per 1,000 at-risk population was observed to get the world on track for the 2020 milestones. Similarly, in recent years, the achievement in reducing malaria cases was levelling off as shown by comparable

figures for 2016-2019 (83). If the current rate of progress persists, the attainment of global milestones for HIV, TB and malaria morbidity and mortality is under doubt.

Far too often, public health complacency towards the reduction of the disease burden causes priority to subside and leads to the emergence of resistant strains and disease resurgence. Emergence of drug-resistant strains for malaria preventive interventions, HIV and TB medicines pose a big challenge to global health and economic security. If these strains are not contained promptly, they will reverse all the gains made so far, with further increase in costs of care (90). For example, in relation to the most commonly used first-line antiretroviral drugs, the rate of resistant strains exceeded 10% (94). Moreover, public health emergencies, such as outbreaks of pandemic diseases like COVID 19, Ebola and influenza in endemic countries with communicable diseases, have a negative effect on the delivery of basic health services, including the ability to control HIV, TB and malaria (79). Hence, stepping up the response to these diseases isn't a choice, and countries need to effectively overcome the challenges to improve population health and wellbeing.

The UN sustainable development goal endorsed in 2015 provides an unprecedented opportunity to boost efforts to reduce morbidity and mortality related to these diseases. SDG 3 target 3.3 of the plan calls the world to "end the epidemics of acquired immunodeficiency syndrome, tuberculosis, malaria and neglected tropical disease by 2030 and combat hepatitis, water-borne diseases and other communicable diseases" (38). Accelerating progress towards this target requires innovative strategies, tools and technologies which includes implementation of high-impact interventions, developments in new medicines, vaccines and diagnostics (79). This effort and investment in the agendas of HIV,TB and malaria are imperative to ensure that the hard-won gains from the global community are not lost (79, 90). The achievement of global targets and ending the epidemics will not only save millions of lives, but it will also reduce poverty and create healthier, more equitable societies (79). Therefore, the fight to end epidemics must be stepped up by countries.

1.6 Country context

1.6.1 Country profile, demography and economy

Ethiopia is Africa's oldest independent country and the second-most populous nation after Nigeria. The country is located on the horn of Africa and bordered by six countries – Eritrea, Kenya, Djibouti, Somalia, South Sudan, and Sudan (Figure 2) (95). The country covers an area of 1.1 million square kilometres. Ethiopia is a country of many nations and nationalities with diverse cultures and heritage.

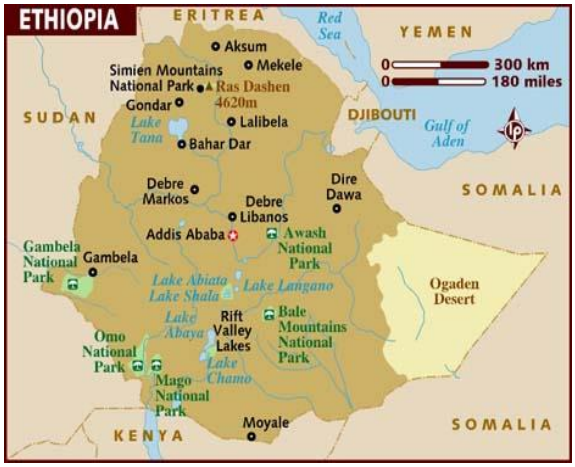


Figure 2: Map of Federal Democratic Republic of Ethiopia.

The projected total population of Ethiopia was 109 million in 2020 as reported by the United Nations Population and Development Division (96). The annual growth rate is 2.6%, increasing at a high rate like other sub-Saharan African countries. Young people constitute the greatest age composition, with 67% of the population under 30 years of age, while women in reproductive age comprised 23.4%. The mean fertility rate is 4.6 child per woman, with considerable differences between rural and urban residents (5.2 versus 2.3), across different regions, the highest was reported in Somali (7.2) and the lowest in Addis Ababa (1.8). The ratio of male to female is almost equal. The majority lives in rural areas (78%), yet recent migration to urban areas has been on the rise (97, 98).

The country achieved substantial economic growth by formulating and implementing ambitious and comprehensive mid-term plans such as the plan for Accelerated and Sustained Development to End Poverty (PASDEP) followed by the Growth and Transformation Plan (GTPI-II), which resulted in the country's steady GDP growth of 9.9% per year with a slight deceleration to 7.7% in 2018. The economic growth is mainly

driven by the construction and service sectors, with the agricultural and manufacturing industries contributing less as the country shifts the economy from agricultural to industrial-led (99). The economic growth, complemented by the Government's pro-poor spending policies, is attributed to an increase in per capita income. Ethiopians' per capita income grew from $ 396 in 2010/11 to $ 794 in 2015/16, resulting in a reduction of population living below the poverty line from 29.6% in 2010/11 to 23.5% in 2015/16 (100). In addition, there was a massive expansion of access to social services that are tied to economic development such as health, sanitation, water and education, as well as infrastructure including highways, railways, telecommunications, and power generation among others. Access to universal primary education and potential coverage of health services exceeded more than 95% and life expectancy exceeded 64 years (78, 101). Notwithstanding this, there are still developmental challenges that affect the path to building sustainable economic growth and reducing poverty in the country. The progress has been challenged by reduced employment opportunities, exports, an under developed private sector, governance and reoccurring drought, which require the country to make substantial progress in this regard in order to sustain the achievements and realise the vision of a middle-income country by 2025 (99).

1.6.2 The health system of Ethiopia

The “health policy of the transitional government of Ethiopia” was formulated in 1993 to expand public access to a core package of primary health services to all segments of the population (102). The policy prioritises the provision of preventive and promotive components of health services using primary healthcare approaches.

A three-tier healthcare delivery model is used throughout the country to ensure access to health services for all segments of the population. Level one comprises a primary health care unit (PHCU) consisting of five satellite health posts, one health centre, and a primary hospital serving up to 5,000, 25,000 (40,000 in urban), and 100,000 people, respectively. The secondary level is a general hospital that serving 1 million people and a tertiary or specialised hospital serves 5 million people (78). Health programmes are planned and implemented through five-year strategic plans in the country. Over the last

three decades, four phases of the Health Sector Development Programme (HSDP I-IV) followed by the Health Sector Transformation Plan (HSTP) guided the implementation and governance of health programmes, which have resulted in improved population health outcomes. Among the gains, the maternal mortality ratio decreased from 676 deaths in 2011 to 401 (per 100,000 live births) in 2017. Similarly, under-five deaths declined from 123 in 2005 to 55 (per 1,000 live births) in 2019. HIV, TB and malaria-related morbidity and mortality have significantly decreased in the country (78, 103). The relevant country health performance measures are depicted in Table 2.

Table 2: Performance of key health indicators, Ethiopia.

Indicator		Year	Value	Source
Maternal and child health				
Under-five mortality rate (per 1,000 live births)		2019	55	(103)
Neonatal mortality rate (per 1,000 live births)		2019	30	(103)
Infant Mortality rate (per 1,000 live births)		2019	43	(103)
Maternal Mortality Ratio (per 100,000 live births)		2017	401	(78)
Total fertility rate (per women)		2016	4.6	(97)
Communicable diseases				
Adult HIV prevalence (%)		2016	0.9	(97)
HIV mortality rate (per 100,000 population)		2018	10	(104)
Estimated number of people needing ART		2018	690,000	(104)
TB incidence rate (per 100,000 population)		2018	151	(82)
TB mortality rate (per 100,000 population)*		2018	22	(82)
Prevalence of malaria (by microscopy)		2016	0.5	(105)
Population at risk of malaria	High, low and free (>1, 0-1 and 0 case per 1,000 population) (%)	2018	27, 41,32	(83)
Malaria mortality rate (per 100,000 population)		2018	4	(83)
General health status				
Life expectancy at birth, total (years)		2016	64	(101)
UHC index		2019	0.43	(78)

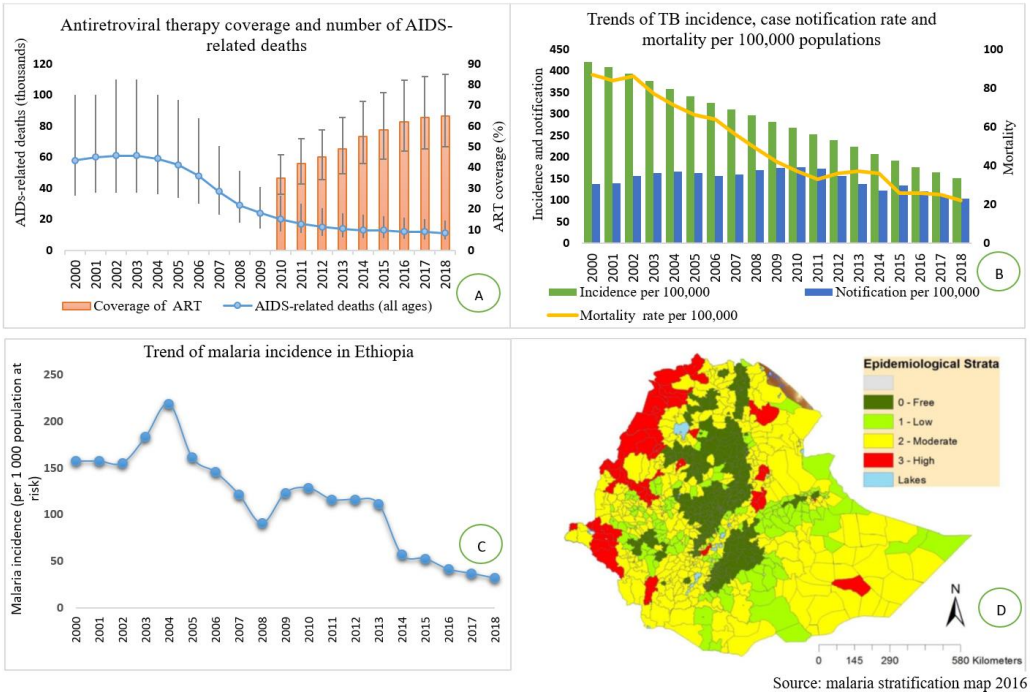
*excludes HIV+TB

However, Ethiopia is still among the countries with very high morbidity and mortality from the triple burden. Preventable communicable diseases, reproductive health-related problems, nutritional disorders and currently rising non-communicable diseases and injuries were the main causes of disease burden in Ethiopia.

1.6.3 Overview of HIV, TB and malaria in Ethiopia

HIV, TB and malaria remain a major public health problem causing ill health and death among tens of thousands of Ethiopians each year. Cognisant of this, the Government has given due attention to the prevention and control of HIV, TB and malaria diseases. The control of these diseases were included among the priority health programmes in all rounds of the country's HSDP and HSTP. In addition, the country have developed and implemented strategies to address these diseases, which are in line with the globally recommended strategies. The disease control programme has also benefited from overall health sector development, particularly through involvement of health extension workers to deliver integrated health promotion and curative services at peripheral health posts and community level.

The country has made substantial gains in reducing the incidence and deaths related to HIV, TB and malaria diseases (106-108). The malaria prevalence (by microscopy) in Ethiopia has declined from 1.3% in 2011 to 0.5% in 2015 (105, 109). The country have a low-intensity generalised HIV-epidemic, where the national adult (age above 15 years) prevalence dropped from 3.5% in 2000 to approximately 1% in 2016 (97). At the same time, the incidence of TB has decreased from 421 to 151 per 100,000 people in Ethiopia, however, the country is still one of the high burdens of TB, TB/HIV and Multi-drug-resistant (MDR) TB (82). The age-standardised HIV and TB mortality rate decreased by 54%, with malaria dropping by more than 90% from 1990 to 2015 (110). Figure 3 demonstrates the performance trend of the major impact measures of these diseases.



Source: malaria stratification map 2016

Figure 3: Trend of communicable disease control performance over 2000-2018, Ethiopia (A: HIV, B: TB, C and D: Malaria).

Scaling up and continued investment in the control of HIV, TB and malaria pay off and saved more lives in the country. In particular, the rise in voluntary counselling and testing, targeted HIV interventions and the implementation of the "test and treat" policy were among the main contributors to the achievement of the HIV programme. Early case detection and expansion of directly observed treatment, short-course (DOTS) and the introduction of new or improved laboratory diagnostics have played a major role in the achievement of TB programme. The implementation of key malaria strategies such as indoor residual spray (IRS), insecticide-treated nets (ITNs), scale-up of rapid malaria diagnostics and treatment of malaria species with highly effective drugs are among the contributing measures to the success of malaria control in Ethiopia (14-16).

Despite progress, much needs to be done and newer challenges are emerging in the country. An estimated 690,000 people live with HIV, 164,900 with all types of TB cases and 2.4 million malaria cases were estimated in 2018, and approximately 40,000 people

die from HIV, TB and malaria diseases each year (82, 83, 104). HIV and TB remain among the top five leading causes of premature death in the country (110). Ethiopia now faces many challenges in achieving the 90-90-90 global targets of HIV and TB. The treatment coverage of HIV and TB is 65% and 69%, respectively (82, 104). The burden of HIV and TB is still high and heterogeneous by sex, agro-ecological areas and population groups (15, 111). On the other hand, malaria is endemic with a marked seasonal and geographic variability in most parts of the country. More than 60% of the total population lives in malaria-risk geographic areas and just 40% of the population slept under insecticide-treated nets the previous night, making malaria the main public health problem in Ethiopia (16, 105, 112). Malaria transmission is extremely variable both spatially and temporally, where areas below 2,000 meters are considered potentially malarious (113, 114). Access to both diagnostic and treatment services of HIV, TB and malaria diseases is not yet optimal, and provision of the treatment service is more provider-centred than person-centred. The impact of these diseases is further exacerbated by poverty and poor health systems of the country.

1.7 Rationale of the study

Efforts have been made to implement effective health policies and reforms to improve the population health in Ethiopia. UHC is seen as an important goal for the health policy of the country. Today, the country is far from reaching universal coverage, even for priority services (73, 78, 115). Coverage of essential services for high priority preventable diseases like HIV, TB and malaria is sub-optimal, resulting in higher financial risks and unfavourable health outcomes among affected individuals and households (78). Evidence on how to achieve universal coverage of these services without financial risk to patients is essential (39). Furthermore, poorer and vulnerable groups, often trapped in cycles of CHE and impoverishment, face barriers to accessing preventive and curative healthcare that they desperately need (115).

The assessment of patient costs, economic returns and health benefits with distributional consequences of continuous expenditure related to HIV, TB and malaria diseases is very important for the effective allocation of available resources and priority setting exercises.

Investment in both preventive and curative interventions to reduce communicable diseases requires a focused approach, driven by empirical evidence (54). However, in most low-income countries, including Ethiopia, the economic burden associated with these diseases and the return on investment from the public financing of major communicable disease interventions have not been fully recognised (6). This may be because the measures of the disease burden have not been complemented by economic terms to augment the existing epidemiological evidence. Hence, the economic burden assessment of communicable diseases would direct health policy by demonstrating where the greatest improvements can be made in ensuring FRP benefits. Health policies that protect individuals and households from the economic burden of diseases are crucial if the government is to achieve the UHC-related SDG goal. Furthermore, linking the evidence of economic burden of these diseases with their potential prevention and treatment by health interventions offers a full picture and judgments as to whether the investments are appropriate for the goal of disease specific programmes.

ECEA is a highly relevant methodology for policy guidance in communicable disease interventions in Ethiopia (68), where disease distribution differs across socio-economic groups, poorer people are disproportionately affected, and often use health services less and spend more as a share of income. Evaluation of the universal public finance of communicable disease interventions on health benefit, equity and FRP domains are essential, especially in Ethiopia, where nearly one-fourth of the population lives below the poverty line and 31% of health expenditure is contributed by OOP (76, 100). The ECEA result will provide evidence of what it takes to deliver such services free-of-charge with high coverage as recommended in the latest EHSP (39). In this study, I tried to address the gap in evidence related to the economic burden of HIV and TB on households, supplemented by evaluating the health gain and FRP benefits of the public financing of malaria and TB intervention across population subgroups, which can help policymakers to consider both health benefits and non-health benefits (i.e. FRP) in priority setting.

2 Objectives of the study

2.1 General objective

The aim of this thesis is to assess patient cost, health gains and financial risk protection of HIV, TB and malaria interventions across socio-economic groups in Ethiopia.

2.2 Specific objective

The specific objectives are as follows:

- To estimate direct cost, indirect cost, catastrophic health expenditures and its determinants across socio-economic groups for household affected by HIV and TB diseases.
- To assess the expected health gains and financial risk protection benefits from the public financing of selected malaria prevention and treatment interventions across socio-economic groups.
- To assess the expected health gains and financial risk protection benefits from the public financing of selected TB interventions across socio-economic groups.

3 Methods

This thesis comprises three interrelated studies that address the specific objectives set out in section 2.2 above. In Paper-I, a nationwide health service utilization and expenditure survey (for HIV) and a health facility-based patient cost survey (for TB) were used to measure patient costs, magnitude and CHE determinants for households affected by the disease. In Paper II-III, cost and expenditure data were linked with the benefits of the universal public finance of communicable disease interventions. Specifically, Paper-II uses ECEA methods to estimate the impact of selected malaria interventions on health, private health expenditure and FRP benefits along with their distributional consequences. Paper-III is based on a modelling study to estimate the impact of universal public finance of selected TB interventions on mortality reduction and FRP benefits across population subgroups in line with the End TB strategy target date (2018-35). This method section initially gives a general description of the study setting, methodological and analytic considerations with relevance across the three Papers (section 3.1 and 3.2), followed by a summary of the specific methods that are unique to each of the Papers (section 3.3).

3.1 Study setting and data

In Paper-I, cross-sectional household data from nine regions and two city administrations were used for the HIV survey and separate sub-national household data collected (as part of this Ph.D. work) from health facilities located in the Oromia and Afar regions were used for the TB survey. The study population for the HIV study was a sample of HIV-positive individuals from all regions and two city administrations. All TB or MDR-TB patients (including children) who received treatment for at least one month from December 2018 to September 2019 in selected health facilities were included for the TB survey. Paper-II employed a static (single year) ECEA model using national malaria estimates and inputs from small scale published studies in the country. The model constitutes the population at risk of malaria, incident cases and one birth cohort. Paper-III was based on a national epidemiological and health impact modelling exercise (TB

Impact Modelling and Estimate (TIME)), followed by a separate ECEA using inputs mainly from the national model and results from Paper-I.

The data sources for these studies were obtained from representative household surveys (e.g. Living Standards Measurement Surveys, Demographic and Health Surveys, National Health Account, Malaria Indicator Survey, etc.). Besides the large-scale surveys, facility-based surveys (exit polls) among service users were used to measure health outcomes. Income/consumption data are collected and used to rank households across socio-economic status. The income distribution would be constructed from primary data or approximated based on Gamma distribution using country inputs such as GDP and Gini coefficient (116). Consumption is based on expenditures on food, non-food and consumer durables (65). The procedure for construction of income or consumption into equal groups or quintiles has been set out in Paper-I: Supplementary Appendix 1. The data inputs and interventions considered in Papers II-III were explored in the main articles of these studies. The following section gives an overview of the methodological and analytical aspects of the three Papers.

3.2 Methodological and analytic considerations

3.2.1 Cost of illness

Assessing the cost of seeking HIV and TB care offers insight into the financial impact of these diseases on patients and families. These costs were mainly divided into direct and indirect costs. Out-of-pocket payments incurred during the course of the disease treatment are considered as direct costs. These costs were further categorised into medical costs that are attributable to medical services and non-medical costs classified as expenses associated with illnesses that are not connected to the direct purchase of medical services (e.g. travel, additional food and miscellaneous costs). Indirect cost is the foregone income or opportunity cost arising from the diseases. In most studies, the household is the preferred choice of analysis, as both direct and indirect cost impact falls on families.

3.2.2 Catastrophic health expenditure

There are various methods for assessing the burden healthcare costs create for household budgets, and this thesis applies metrics and definitions of CHE that have been commonly used in previous studies (67). Some define CHE as OOP for healthcare exceeding a predefined threshold (i.e. 10% or 25%) of income or consumption in a given period (22). Others assess CHE in relation to the available income after fulfilling basic needs such as food and accommodation, and defines CHE as OOP exceeding 40% of the capacity to pay. The former assumes the whole budget of a household is available for healthcare expenses and typically used to measure progress related to the SDGs UHC indicator, while the latter is driven by households' ability to pay for healthcare and better differentiates between the poor and the rich (26, 72, 117). The proportion of healthcare expenses from the total budget illustrates the degree to which individuals lack FRP and are influenced by the choice of the threshold used to measure CHE. Specific disease programmes, such as TB, use a different approach for estimation of CHE than the SDG monitoring framework (SDG 3.8.2). For instance, the TB-specific 'catastrophic total cost' is one of the main targets of End TB strategy and its measurement involves inclusion of both direct and indirect costs. The measurement of the indicator is confined to a population seeking care under the national TB network. Whereas, the CHE measure in the SDG monitoring framework mainly focuses on direct medical care expenses and excludes loss of earnings due to the disease. The latter indicator incorporate individuals who are unable to visit or afford to pay for healthcare (69, 118). For the estimation of CHE in Papers I-III, a range of thresholds were used to facilitate comparisons with previous studies. In Papers II-III, the impact of the universal public finance of malaria and TB interventions on FRP benefits was investigated using the difference in the number of CHEs stratified by the income quintiles prior to and after the policy was implemented.

3.2.3 Health equity analysis

Health equity analysis illustrates the disparities in the health and non-health outcomes across the various subgroups. This type of analysis helps to properly identify coverage

gaps and progress towards equitable access. This study mainly focuses on equity analysis across socio-economic groups, where expected distributive health and FRP benefits of interventions are assessed. The analysis demonstrates how the outcome measures such as deaths, OOP payment and CHE, are equitably distributed across income quintiles. Universal public finance benefits of TB and malaria interventions in preventing these outcomes across income quintiles were also estimated. The final health equity result was reported using tables and graphs, rate ratios, concentration curves and concentration indices. The concentration curve visually maps disparities in outcomes through socioeconomic status, and the concentration index numerically estimates the extent of health inequality on a scale from 0 (full equality) to 1 (full inequality) (65).

3.2.4 Extended Cost-Effectiveness Analysis

The ECEA methods examine both the health and non-health outcome of health policies or interventions (of either preventive or curative). The method uses a dashboard approach that explicitly quantifies the impact of health policies with respect to health gains, crowding out of private spending and FRP. ECEA generates the results using measures such as deaths or DALY averted, private expenditures (i.e. OOP) averted and FRP offered by the policy (i.e. measured using cases of CHE and poverty cases averted and money-metric value of insurance provided). It also illustrates the benefits of investments at the national or sub-national level by equity relevant strata (i.e., income quintiles, gender, marginalised populations and geography). Furthermore, the provision of public finance as a policy instrument entails additional cost or investment that would be quantified from a government or provider perspective (i.e. net policy costs). The outputs from ECEA provide information to decision-makers on how each policy intervention affects different segments of the population (68).

In pursuing ECEA, the first step is to define the problem of existing inequalities in health outcomes or coverage, the extent of spending on OOPs, and impoverishment. The next step is to identify a policy or intervention that reduces inequalities in health outcomes and reduces financial risks for households. Thirdly, identifying and defining the target population or group for which the health policy or intervention is being implemented.

Finally, identifying the policy instrument (e.g. public finance, cash transfer) which is basically intended to improve the uptake of the effective interventions. Each step needs inputs disaggregated by population subgroups (i.e. epidemiology/demography, interventions, total costs including OOP and income) to assess the aggregate and distributional impact of the policy (Figure 4) (68).

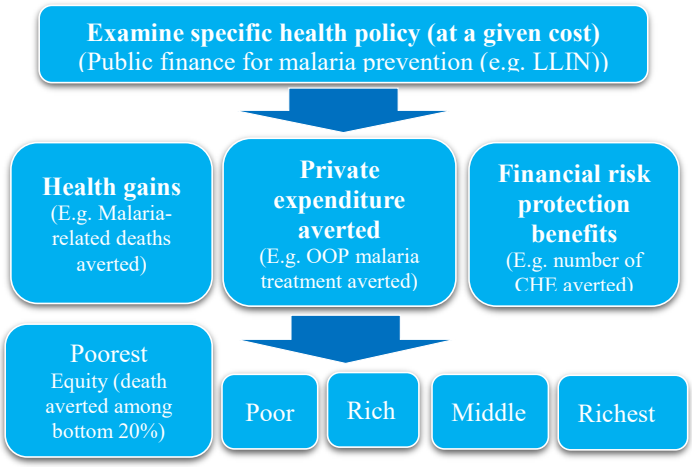


Figure 4: Conceptual structure of the Extended Cost-Effectiveness Analysis.

3.2.5 Outcome measures

In Paper-I, patient cost and CHE were used as the main outcome measures. The costs are further stratified and reported by the model of care, severity of disease, provider type and socio-economic status. The outcome measures in Paper-II are deaths, private spending and CHE averted, including net government costs. Similarly, deaths and CHE averted were used as an outcome in Paper-III and cumulatively reported over the period from 2018 to 2035.

3.3 Method used in the specific Papers

3.3.1 Paper-I: Financial burden of HIV and TB among patients in Ethiopia: a cross-sectional survey.

3.3.1.1 Study population, design, and data collection

In this study, two data sources were used, one for a HIV survey and another for a TB survey. For HIV, nationwide (i.e., nine regions and two city administrations) household data were employed to estimate direct, indirect costs and CHE among People Living with HIV across income quintiles. A total sample size of 4,208 was determined. A two-stage stratified cluster sampling approach was employed. In the first stage, out of a total of 588 associations, a sample of 105 HIV associations was randomly selected and allocated to each region proportionally to their population sizes (i.e. number of associations). In the second stage, 40 HIV participants per each associations were selected for interview, for a total of 4,171. A total of 1,006 participants had HIV-related care and were included in this study. The study included individuals older than 18 years. The data were collected from mid-September until mid-October 2016.

The TB survey is carried out in selected zones of the Afar (Zone 3) and Oromia (Adama special zone and Jimma zone) regions, representing more than 4 million people. The three zones were purposely selected to illustrate the country's geographical and socio-economic heterogeneity. A systematic random sampling was used to select 27 public health facilities from the three zones. The estimated total TB sample size was 818 and allocated proportionally to the TB caseload review of selected health facilities. This ensured that all TB cases across all eligible health facilities had an equal chance of being selected. A total of 787 TB patients receiving at least 1 month of treatment in selected health facilities were sampled and interviewed consecutively until the required sample size was met. The data collection period was from December 2018 to September 2019 and the response rate was above 95%. Figure 5 below presents a map of the study area for both the HIV and TB surveys.

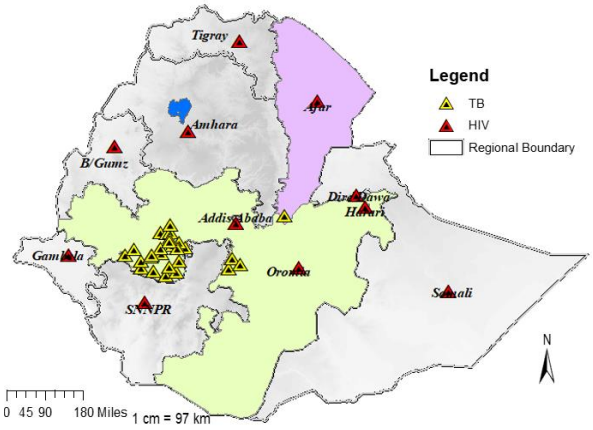


Figure 5: Map of the study area for both the HIV and TB surveys.

A questionnaire adapted from a standard costing tool was used to collect a wide range of variables including socio-demographic, clinical information, patient costs, time losses, consumptions, income, asset and coping measures (119, 120). The questionnaire was translated into local languages, subsequently pre-tested and amended.

3.3.1.2 Costing

The healthcare costs of the two diseases were evaluated from the patient perspectives. For HIV, mainly expenditure related to routine care, co-morbidities and management of opportunistic infection was considered. Expenditure was collected for outpatient and inpatient visits covering a period of one month and six months prior to the survey, respectively. Whereas, for TB episodes, expenditure from the symptom onset, diagnosis and treatment completion has been included.

The direct cost was measured as expenses covering consultations, medicines, laboratory tests and imaging, hospital days and travel, food/nutritional supplements and accommodation, etc. excluding reimbursements while seeking HIV and TB care. Indirect costs were measured as foregone days due to inability to work, hospitalisation, travel to/from the health facility and receiving/waiting for care. In addition, the indirect cost contains guardian time for TB. The reported time loss was summed up to obtain the total time lost. Finally, the indirect costs were valued by multiplying the total time lost with an hourly wage rate derived from monthly income (for HIV)/consumption (for TB) by

assuming 22 working days per month and 8 hours a day. The combination of direct and indirect costs would provide total cost. An average of four HIV outpatient visits and single TB episode outpatient visits was considered to annualise the cost. The average outpatient HIV visits per year were extrapolated based on per capita healthcare visits an individual made over the last month. The cost related to TB care was extrapolated for the full duration of the TB episode, based on the treatment they were in, and retrospectively reported cost data.

All costs were collected in local currency (i.e. Ethiopian Birr) and converted to the US $ with the 2019 exchange rate of $1= 29.1468 Ethiopian Birr (108). The cost for HIV care was first converted to a reference period (2019), using the consumer price index of Ethiopia (121). Measurement of living standards depends on the availability of data, where household income (in-kind and cash) for HIV and total consumption for TB was used and scaled to adult equivalence (see Paper-I: Supplementary appendix 1 for more details).

3.3.1.3 Data analysis

3.3.1.3.1 CHE incidence and intensity estimation

This study measured the economic burden related to seeking HIV and TB care. The incidence of CHE is estimated by using a cut point of 10% of household income or consumption. In addition, further analysis was conducted at a threshold of 20% of both OOP and total cost, and also using 40% of non-food spending. Moreover, two other indicators "over-shoot" and "mean positive over-shoot" were reported as a metric of CHE intensity (depth). Overshoot measures the degree to which the average HIV and TB care expenses in the whole sample surpassed the threshold; mean positive overshoot measures the degree to which the average expense for CHE-affected households surpassed the threshold.

3.3.1.3.2 Health inequality measures (Concentration curve and index)

A concentration curve was used to plot the cumulative percentage of people seeking HIV and TB care on the x-axis (i.e. ranked from the poorest to the richest) and the cumulative percentage of patient cost or share of OOP on the y-axis to assess the health inequality across income quintiles. The patient cost or share of OOP is more concentrated among the poorest households when the curve lies further above the 45 ° line of equality and vice versa. Similarly, the concentration index ranges from -1 to 1. A negative value, at a minimum of -1, indicates that the patient cost or share of OOP related to HIV and TB service is more concentrated among poor households (i.e. the concentration curve is at the top of the equality line), while a positive value indicates the opposite. A value of '0' implies independence of inequality. In addition, a pen's parade plots household income or consumption before and after HIV and TB related OOP expenditures. Furthermore, the interval plot (with 95% confidence interval for the mean) has been used to plot the incidence and intensity of HIV and TB-related CHE across income quintiles.

3.3.1.3.3 Statistical analysis

Descriptive statistics of demographic, socio-economic, clinically relevant variables, and patient costs were reported for HIV and TB participants. The Kruskal-Wallis test was employed to assess patient cost disparities across income quintiles. Multivariate logistic regression was employed to identify the determinants of CHE by incorporating significant variables from the univariate analysis. A stepwise regression method was used to construct the final model. The Hosmer-Lemeshow test and receiver operating characteristic curve was used to check the goodness of fit and the predictive power of the final model (122). A statistical test was conducted at 5% level of significance for all tests. The analysis in Paper-I was performed using STATA V.16.

3.3.2 Paper-II. Health gains and financial risk protection of selected malaria interventions in Ethiopia: an extended cost-effectiveness analysis.

3.3.2.1 Interventions and data inputs

In Paper II, ECEA was used to evaluate the health and non-health benefits of selected malaria interventions in Ethiopia. The study assessed four malaria disease prevention and control interventions, which include i) artemisinin-based combination therapy (ACT), ii) long-lasting insecticide-treated bed nets (LLIN), iii) indoor residual spraying, and iv) malaria vaccine. Unlike the first three, the last intervention was a hypothetical malaria intervention that had not been introduced in the country at that time. An ECEA model was employed to determine the number of malaria-related deaths and OOP spending averted, the FRP provided and the government cost associated with universal public finance of selected malaria intervention across income quintiles in Ethiopia.

The target for LLIN and IRS intervention was population residing in malaria at-risk areas that constituted 60% of the total population. All malaria cases reported in at-risk areas in 2016 were eligible for ACT. Similarly, the target for a malaria vaccine was one birth cohort (born in 2016) which was followed for five years to capture the full effect of the vaccine. The target population was distributed equally through income quintiles for all interventions to assess the equity of the health policies. The number of malaria susceptible infants across income quintiles was approached for the vaccine through the distribution of total fertility rates. The input related to malaria prevalence distribution by income quintiles for at-risk populations was proxied by the gradient of malaria prevalence in the general population. The percentage of hospital admissions related to malaria was extracted from existing literature and disaggregated by population subgroups based on malaria prevalence across income quintiles (123). For both outpatient and inpatient cases, case fatality ratio (CFR) was derived from literature and assumed to be constant across quintiles. The baseline malaria-related deaths were then distributed across income quintiles for all interventions (except vaccine) (see Paper II, Additional appendix for details).

In the case of the vaccine, the total malaria deaths among children under-five was obtained by multiplying the number of deaths from malaria in the general population by the proportion of under-five malaria deaths (124, 125). In particular, the distribution of malaria-related deaths by income quintiles requires proxy inputs (such as prevalence, treatment coverage, child mortality and efficacy) that are associated with malaria-related deaths and differ across income quintiles except for efficacy measure (126). In addition, under-five deaths from malaria was disaggregated by age group, as the vaccines efficacy decreases over time (124, 125). During the follow-up period, a Weibull decay function was used to represent the waning effect of the malaria vaccine. The birth cohort received three doses of malaria vaccine within 6–9 months, with protection beginning at the age of 9 months (127).

An incremental coverage of 10% has been chosen for all malaria interventions and is presumed to be achievable within 1 year or a short period. In addition, coverage of fully immunised children with a scale of 0 to 33% is considered for malaria vaccines (97). The costs incurred by the household and the healthcare system when an individual seeks outpatient/inpatient malaria care across income quintiles were extracted from previous studies conducted in the country (21, 128).

3.3.2.2 Health benefits

The health benefit was measured in terms of deaths averted. Firstly, the potential number of deaths that would have occurred in each income quintile at the existing coverage levels was estimated for each malaria intervention (2016). Secondly, using the data on malaria incidence, CFR, intervention efficacy and incremental coverage by income quintiles, and the magnitude and distribution of malaria deaths averted for each intervention after universal public finance were estimated (see Paper II, Additional appendix for details).

3.3.2.3 Private expenditure averted

In estimating private expenditures averted, universal public finance was assumed to remove before the policy co-payment (OOP spending) for treatment interventions and prevents a subset of malaria cases and associated private expenditure for preventive

interventions. From the perspective of the households, the level of private expenditure averted (by income groups) on malaria care after the public finance of malaria interventions was estimated and reflects cost savings. Private OOP expenses averted depend on: target population, healthcare use, incremental coverage, OOP costs and effectiveness of preventive interventions (see detailed mathematical equation in Paper II, Additional appendix).

3.3.2.4 Financial risk protection benefits

In order to estimate CHE under the baseline and each policy intervention scenario, two methods were used. First, CHE was determined by comparing household total OOP expenses against a cut of value of 10% of total consumption. Alternatively, 40% of capacity to pay (i.e. total household non-food consumption) were used to define CHE for this particular study (22, 26). The annual household consumption as income proxy was obtained from the 2016 consumption and expenditure survey (129). Universal public finance would reduce the malaria incidence and related OOP spending, thus avoiding the occurrence of many CHE cases. Subsequently, for each malaria intervention, the FRP offered to households was quantified in terms of the cases of CHE averted, calculated as the difference in cases of CHE before and after universal public finance (see Additional Appendix for information in Paper II).

3.3.2.5 Programme costs

The programme costs were any government costs incurred while the four malaria interventions were being scaled-up through universal public financing. The intervention costs include net price and distribution costs for LLIN; insecticide costs, spray campaign activities, labour and capital costs for IRS; vaccine prices, supplies, training, transportation and waste management costs for the vaccine, and labour, medication and supplies for ACT. The total costs consider the target population, intervention coverage and unit cost of the interventions (see the detailed mathematical equation in Paper II, Additional appendix). Patients and the healthcare system costs were converted for the year 2016 using Ethiopia's GDP deflator before analysis (130). A one-way sensitivity analysis was carried out to check the robustness of the findings.

3.3.3 Paper-III. Mortality reduction and FRP benefits of expanded TB control in Ethiopia: findings from a modelling study.

3.3.3.1 Model input and interventions

In Paper-III, a compartmental transmission model (i.e. TIME Version 5.76 nested in the spectrum software package) was used to generate projection of TB incidence, prevalence and mortality for both drug-susceptible (DS-TB) and MDR-TB burden during the period from 2018-2035. The TIME model is used to project the epidemiological effect of TB interventions over time, and a detailed methodological overview is described in previous literature (131). The TIME model automatically incorporates TB impact measures from the WHO global database and HIV impact estimates from UNAIDS and population values from the UN Population Division. Estimates of prevalence were extracted from the national TB prevalence survey in Ethiopia. Key pathogenetic and epidemiological parameters were accessed from published literature and surveys. The programmatic and laboratory-related performances were extracted from country reports and expert opinion from the national TB programme. The baseline model was calibrated manually and fitted to TB prevalence, incidence and mortality with past trends from 2000-17. The baseline model was based on the existing TB performance in the country and assumed that the epidemiological and programmatic parameters were still at their current levels for 2018-2035.

In accordance with the post-2015 End TB strategy, and based on availability of required data for analysis, three TB prevention and control strategies were modelled in the intervention scenario and compared with the existing TB control performance (base-case). The interventions include implementation of active case finding (Int1); enhanced implementation of DOTS for DS-TB (Int2), and improved MDR-TB diagnosis and treatment (Int3), most of which are currently being implemented in the country. The primary aim of these interventions was to find TB cases (Int1), link them to care and ensure successful treatment (Int2-3). Int1 is primarily done through the involvement of health extension workers to educate, identify and refer presumptive TB cases for further evaluation through house-to-house visits, contact investigations and provision of proper treatment follow-up for diagnosed patients. Int2 mainly involve health workers training

on TB protocols, patient education, care and adherence counselling for drug-susceptible cases. Specifically, Int3 focuses on the implementation of robust case finding strategies such as Xpert for diagnosis, instituting an improved model of care, provision of effective treatment and adherence counseling for MDR-TB cases. Using the calibrated model, the impact of the three TB control interventions during the period (2018-2035) was projected. The increased coverage due to public financing was determined through consultation and discussion with national TB experts and assumed to be achieved by 2025 (2030 for Int3). Linear scale-up was applied for all intervention coverage from 2018-25 (2018-30 for Int3) and presumed constant values from 2025 onward (2030 onwards for Int3). Several model parameters were affected following each intervention. For example, for enhanced MDR-TB care or Int3, three different model probabilities were mainly assumed to change (treatment success rate, linkage to care and drug susceptibility testing). The detailed inputs and assumed coverage due to universal public finance can be found in Paper III-Table 1 and 2. The projected outcomes, over 18 years, include: number of active TB cases, number of treated TB cases, total diagnostic test performed, the mean duration of diseases, number of TB-related deaths for base-cases and intervention scenarios.

Evidence on TB prevalence disaggregated by quintile was not available in the country. The distribution of TB cases by quintile was estimated using a methodology described in the previously published study (132). Firstly, a set of five proxy factors (i.e. HIV, smoking, the prevalence of malnutrition, overcrowding and history of contact) that are associated with increased likelihood of contracting TB have been identified. Then, TB cases are distributed across income quintile based on two inputs: i) the importance of risk factor in increasing TB disease (i.e. relative risk of these risk factors) and ii) the risk factor prevalence obtained from the Ethiopian Demographic and Health Surveys (EDHS 2016) (97, 133). Subsequently, the distribution of TB cases across income quintiles was made based on the prevalence and the relative weight assigned to each risk factor for TB (see Paper III: Supplementary Appendix). Probability of healthcare use across income quintile was also extracted from published literature (134).

3.3.3.2 Estimation of health benefits

The reduction in TB-related deaths from enhanced coverage of Int1-3 across socio-economic groups was assessed during the years 2018-35 (i.e. in line with End TB strategy target date). As there is no evidence of TB mortality by income quintile in Ethiopia, the total TB deaths at the base-case and intervention scenario (i.e. output from the TIME modelling) was distributed using a method outlined in previous literature (126). Specifically, the distribution of TB deaths by income quintiles for each year and cumulatively was estimated in 2018–35 by applying the coverage gradients of the probability of seeking TB care, mortality rate by quintile (i.e. a proxy for the probability of dying from TB) and the effectiveness of TB treatment (see Paper III: Supplementary Appendix for detail). In the absence of evidence regarding which proxy parameters represent more of the quantile share, an average based on the three proxies was calculated to obtain a single estimate of TB mortality in each of the five quintiles. Then, the number of deaths across income quintile for the base-case and intervention scenario was estimated. The total deaths averted is the difference between total deaths at baseline and under each policy intervention per quintile over 2018-2035.

3.3.3.3 Estimation of FRP benefits

Estimates of patient costs, both direct and indirect costs incurred by patients, were imputed from recently published Paper-I results (135). The patient cost data are disaggregated further by type of TB cases (i.e. DS- and MDR-TB care). Similarly, distribution of income is proxied using a simulated gamma distribution constructed from the gross domestic product per capita and the Gini coefficient of Ethiopia (116). All costs were expressed in 2019 United States dollars.

Financial risk protection benefits from public financing mainly occurred from a reduction in TB cases and related costs (Int-1) that would have occurred without intervention, and from improved treatment and linkage to care (Int2-3) that reduce the lost to follow-up, duration of contagiousness, and secondary cases. The FRP was estimated using the number of cases of CHE averted. In this study, CHE (also called catastrophic total costs) for TB was counted when the total cost (direct and indirect costs

combined) exceeded 20% of household income (see Paper III: Supplementary Appendix for details) (118). In line with the literature, other thresholds for CHE that generally lies between 10-40% of total household expenditure were also explored in the scenario analysis.

Cases of CHE incurred under the base-case and each intervention are calculated for each year and cumulatively in 2018–35. Cases of CHE averted by each intervention were calculated by subtracting the number of households incurring CHE in the intervention scenario from the base-case.

3.3.3.4 Scenario analysis

In this study, various scenarios were performed to check the robustness of the result in relation to the model parameters. In the sensitivity analysis, for deaths averted, the effect of varying parameters used to distribute TB-related mortality such as effectiveness of treatment, healthcare use, and mortality estimates were investigated. For CHE averted, the influence of varying prevalence of TB, threshold for CHE, healthcare use, and patient costs was examined. Data analyses were carried out using R-Studio (version 4.0.0).

3.4 Ethical consideration

Ethical approval for Paper-I was obtained from the National Committee for Medical and Health Research Ethics in Norway (2018/1647/REK) and from the Ethiopian Public Health Institute (EPHI-IRB-121-2018). Official letters bearing a request for collaboration were written to the Oromia and Afar Regional Health Bureaus. In collaboration with respective zonal health offices, the regions granted permission to undertake the TB study. All participants were informed about the purpose and expected outcome of the study, and informed consent was obtained before each interview. All the information collected through the study was kept confidential, and analysis was carried out without revealing the identity of individuals to ensure privacy. Papers II-III did not require ethical approval, as the studies depends on secondary data and findings from Paper-I which are publicly available.

4 Summary of results

4.1 Paper-I. Economic burden of HIV and TB.

Socio-demographic and clinical characteristics

The socio-demographic and clinical characteristics of HIV and TB study participants are summarised in Table 1 of Paper-I, but briefly, females account for 75% and 50% of the total HIV and TB study participants, respectively. More than two-thirds of the participants were between 25 and 44 years old for HIV and below 34 years for TB. The median household size was four (inter-quartile range (IQR), HIV: 3 to 5, IQR, TB: 3 to 6). The average (standard deviation (SD)) annual household income/consumption for HIV was $ 1,188 ($ 1,288) and TB was $ 545 ($ 462). About 22% of HIV and 6% of TB participants had both outpatient and inpatient visits. During the study, only 2% of HIV and 6% of TB patients were enrolled in a community health insurance scheme.

HIV and TB patient costs

The mean (SD) cost of care for HIV was $ 78 ($ 170) per year and $ 115 ($ 118) per TB episode (with 4 times higher cost for drug-resistant TB). The major cost drivers were medical costs for HIV, while non-medical costs and productivity loss for TB. The total HIV and TB patient cost, on average, was equivalent to 7% and 21% of their annual income, respectively. The direct cost of HIV and TB accounted for 69% and 46% of the total cost, respectively. Medical costs accounted for 68% and 38% of HIV and TB direct costs, respectively (Figure 6). The total mean (SD) cost for hospitalisation episodes is HIV: $ 96 ($ 139), TB: $ 105 ($ 78), and for TB/HIV co-infection is $ 188 ($ 33).

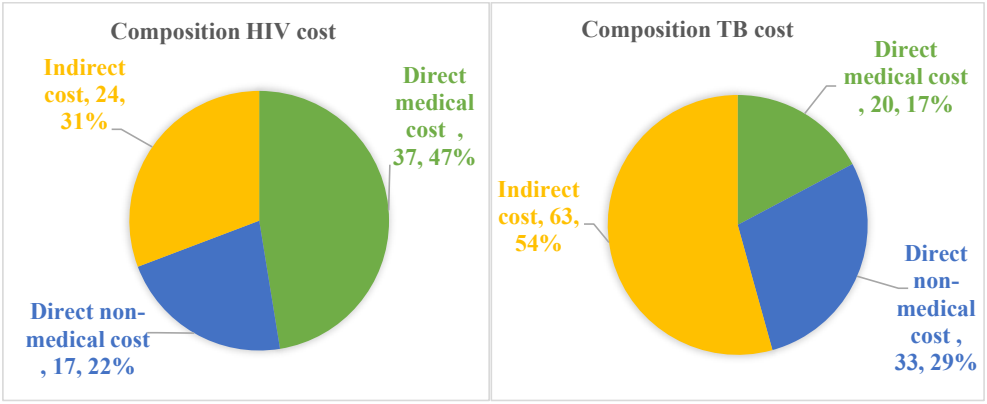


Figure 6: Household direct medical, non-medical and indirect cost of HIV and TB care in Ethiopia (expressed in $).

Incidence and inequality in financial risks

The total mean (SD) cost also varies across socio-economic status, from the lowest to the highest income or consumption quintile ([HIV: ranges $ 53 ($ 97) to $ 133 ($ 262)], [TB: ranges $ 50 ($ 44) to $ 202 ($ 189)]). The concentration index of the total cost of HIV and TB care against the ranked living standards, starting with the poorest and finishing with the richest, was 0.175 and 0.251, respectively. Similarly, the concentration index for the share of OOP payment is -0.476 and -0.219, respectively. These indicate that, in absolute terms, the rich spend more on HIV and TB care, but in relative terms, the poor spend more as a share of total income or consumption.

The incidence of CHE occurred in one-fifth (20%) of HIV households (43% of the poorest to 4% of the richest income quintile, $p<0.001$) and that of TB households was 40% (where it reaches 58% in the poorest and 20% in the richest income quintile, $p<0.001$) (Figure 7). Furthermore, the incidence was considerably higher for inpatient HIV care (33%) and (94%) for inpatient TB care, for individuals co-infected with TB/HIV (48%), and for patients with MDR-TB (62%).

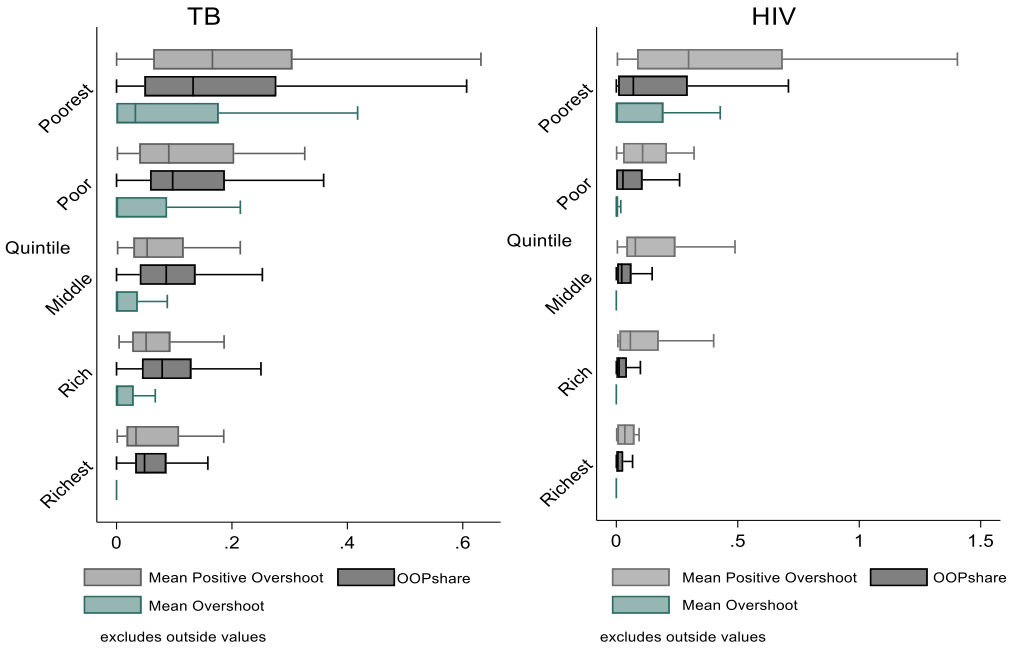


Figure 7: Box plot of OOP share, mean overshoot and mean positive overshoot at 10% threshold associated with HIV and TB care across income quintiles.

In a multivariate analysis significant determinant factors for incurring CHE common to both HIV and TB disease were being hospitalised, having frequent health facility visits and living in the poor or poorest households. In addition, diagnosis at the private health facility, type of TB and co-infection were additional determinant factors for TB (see Paper I, Table 4).

4.2 Paper-II. Health gains and financial risk protection of malaria interventions.

Health benefits

Increasing the coverage for ACT, LLINs, IRS and malaria vaccine by 10% through universal public finance accounted for 358, 188, 107 and 38 malaria deaths averted per year among at-risk population, respectively. In contrast to the other malaria interventions evaluated here, LLIN and ACT accounted for a higher proportion of the deaths averted (Table 3).

In addition, there are variations in the magnitude of deaths averted through income quintiles for all malaria interventions. For instance, ACT, LLINs, IRS and malaria vaccine save more lives among the poorest quintile (i.e. 30% of deaths averted), mainly attributed to the high prevalence of malaria and its risk factors in this group. Almost half of the deaths averted occurred in the lowest socio-economic groups (i.e. the poorest two quintiles). To consider the relative effectiveness of malaria interventions, the number of deaths averted per 1 million dollars spent was estimated, which differs greatly with malaria interventions, from less than 5 deaths averted for IRS to more than 60 deaths averted for the ACT (see Paper II, Additional appendix, Figs. S1-S3).

Private expenditure averted

The four malaria interventions (i.e. ACT, LLIN, IRS and malaria vaccination) would avert approximately $ 4,277,000, $ 214,000, $ 122,000 and $ 15,000 of private health expenditure, respectively. The gains in private expenditures were evenly distributed (i.e. flat) across income quintiles. The even trend of private expenditure averted across income quintile was a reflection of the uniform gradient of patient costs by income quintile, the downward trend in the distribution of the prevalence of malaria from poorest to richest, and the rise in the use of healthcare from poorest to richest (Table 3).

Financial risk protection

The four malaria interventions led to a reduction in the number of CHEs. The largest proportion of cases of CHE averted per year was generated by ACT 440 (10% of the base-case), followed by LLINs 220 (5%), IRS 125 (3%) and vaccination against malaria accounted for 18 (2%). The majority of cases of CHE averted occurred in the poorest quintile and very few to nil were averted in the richest quintiles (Table 3).

Table 3: Distribution of deaths averted, private expenditure averted and CHE averted by each malaria intervention per income quintile in Ethiopia.

Intervention	Outcome	Total	Q1	Q2	Q3	Q4	Q5
Artemisinin-based	Deaths averted	358	107	71	82	50	47
	Private expenditure averted	4,277,000	966,210	847,470	891,970	789,080	782,700

combination treatment (ACT)	CHE averted	440	182	106	152	-	-
Long-lasting Insecticidal	Deaths averted	188	56	38	43	26	25
	Private expenditure averted	214,000	48,310	42,380	44,600	39,460	39,140
	CHE averted	220	91	53	76	-	-
Indoor residual spray	Deaths averted	107	32	21	25	15	14
	Private expenditure averted	122,000	27,540	24,150	25,420	22,490	22,310
	CHE averted	125	52	30	43	-	-
Malaria Vaccine	Deaths averted	38	11	8	8	6	4
	Private expenditure averted	15,000	4,880	3,660	2,560	2,280	1,220
	CHE averted	18	9	5	4	-	-

Q1, poorest income quintile; Q5, richest income quintile.

Government Expenditures

A 10% incremental coverage of ACT, LLIN, IRS and the malaria vaccine through universal public finance costs the Government $5.7, 16.5, 32.6, and 5.1 million, respectively. The scale-up of the IRS was the most costly intervention, accounting for twice the expense of LLIN.

4.3 Paper-III. Mortality reduction and FRP of expanded TB control.

In this section, the projected numbers of deaths and cases of CHE averted were reported, as compared to the baseline (i.e. if the existing TB control programme performance remains the same during the period from 2018-35). Int1 was primarily presumed to increase the screening rate by 25% over the follow-up period, in addition to the effect on other parameters. Similarly, Int2 and Int3 were mainly assumed to improve the linkage and treatment success rates for DS-TB (to 95% in 2025) and MDR-TB (to 95% in 2030) from a varying baseline coverage according to HIV status.

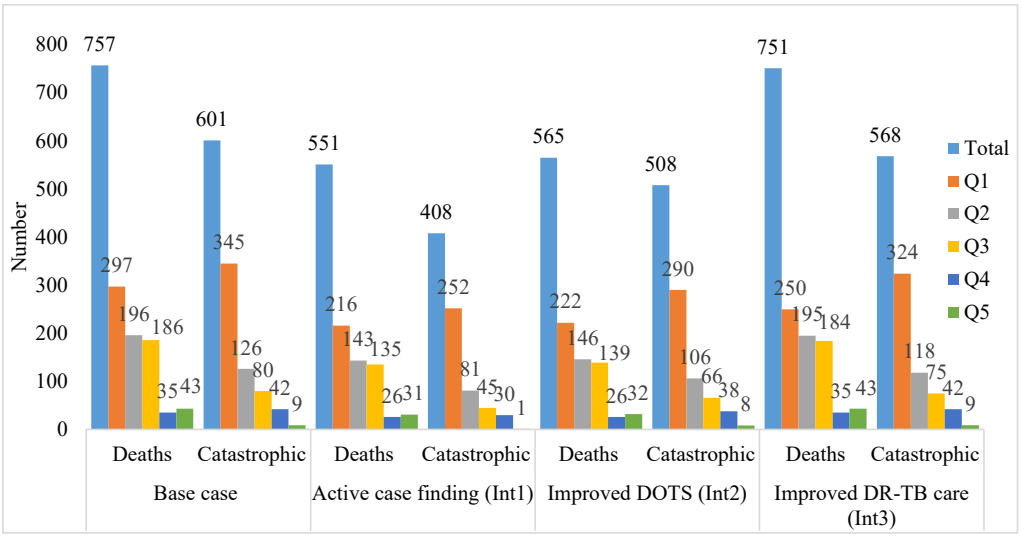
Health benefits

Deaths and CHE cases occurring at baseline and with interventions

In Ethiopia, TB-related deaths are projected to be 757,000 without intervention during 2018-2035. The largest proportion of TB deaths were projected to occur in the poorest quintiles (40%) compared to the richest quintiles (6%). Similarly, at baseline, the estimated number of households that incurred TB related CHE was approximately 601,000 over the same period. Catastrophic healthcare costs have occurred in all quintiles and the poorest quintile accounts for the largest percentage of the overall CHE (57%) compared to the richest quintile (2%). The bottom two income quintiles accounted for the largest proportion of cases of CHE (75%) compared to those in the richest two income quintiles (<10%), where the risk and prevalence of TB were higher in the former group (Figure 8).

Deaths and cases of CHE averted with TB interventions

Implementing active case finding (Int1) over the follow-up period would avert about 206,000 TB deaths (i.e. 27% of the base-case total deaths) and 193,000 cases of CHE (i.e. 32% of the base case catastrophic cases). The enhanced implementation of DOTS (Int2) averts about 192,000 TB deaths (25% of the base-case total deaths) and 93,000 cases of CHE (15% of the base-case catastrophic cases). The improvements in MDR-TB care (Int3) cumulatively avert around 6,300 TB deaths (up to 1% of the base-case total deaths) and 33,000 cases of CHE (up to 6% of all catastrophic cases incurred in the base-case) (Figure 8). These findings also indicate the marked disparities in CHE risk and access to care across income quintiles.



Q1: poorest income quintile; Q5: richest income quintile.

Figure 8: Estimated number of households (in thousands) incurring TB-related deaths and CHE across income quintiles at a 20% threshold over 2018-2035, in Ethiopia.

The trend of deaths and CHE averted increased overtime for active case finding (Int1) and enhanced DOTS implementation (Int2) with immediate gain to be realised, but that of improvement in MDR-TB care (Int3) was marginal (Figure 9 and 10).

Deaths and cases of CHE averted across socio-economic groups

The deaths and CHE averted from the universal public finance of TB interventions (Int1-3) vary across socio-economic groups. The poorest quintile, as they are more likely to acquire TB despite their low care-seeking behaviour, accounted for the largest share of deaths and CHE averted. The implementation of active case finding (Int1) and enhanced implementation of DOTS (Int2) averted about 39% of deaths occurring in the poorest quintile compared to 6% in the richest quintile. In addition, the improvements in MDR-TB care (Int3) would cumulatively lead to a 34% reduction in deaths that accrue to the poorest quintile, while only 10% in the richest quintile. More than half of the deaths averted by all TB interventions concentrated among the bottom two quintiles.

Similarly, enhanced implementation of active case finding would avert a higher proportion of TB-related CHE (48%) among the poorest quintiles as compared to only

4% in the richest quintile. Implementation of enhanced DOTS and improved MDR-TB care would each avert approximately 60-65% of cases of CHE in the poorest quintile compared to 0-1% in the richest quintile, respectively. In terms of FRP, households in the poorest two quintiles benefitted from all three TB interventions, where 70-85% of CHE cases were averted in this subgroup (Figures 9 & 10).

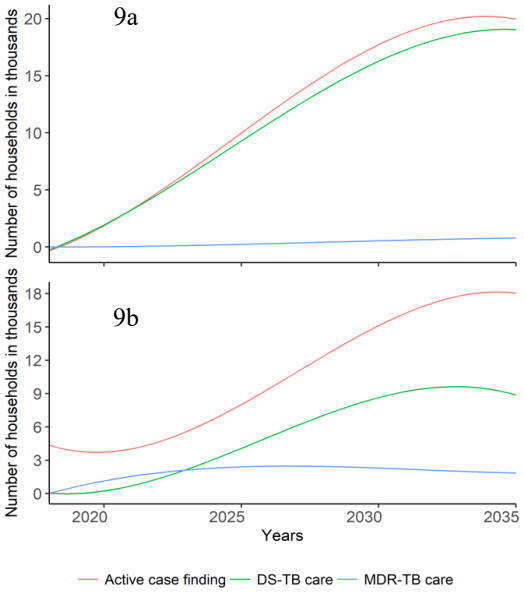


Figure 9: Total number of deaths averted (in 1,000s) (9a) and incidence of CHE averted (in 1,000s) (9b) over 18 years among households in Ethiopia through scale-up of core TB interventions.

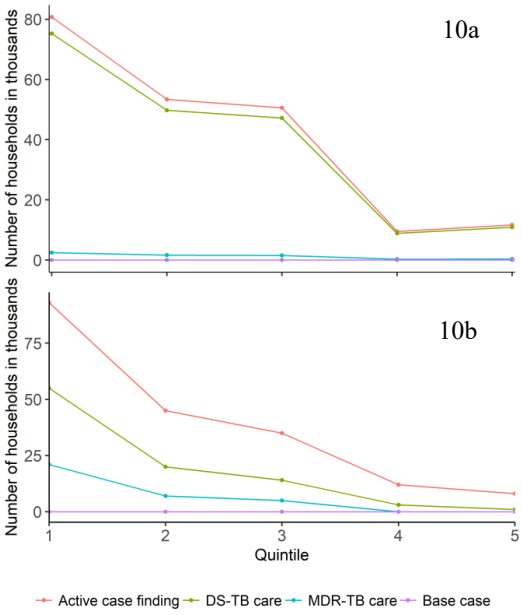


Figure 10: Cumulative number of households per quintile with deaths averted (in 1,000s) (10a) and the number of CHEs averted (in 1,000s) (10b) through scale-up of core TB interventions in Ethiopia.

5 Discussion

Priority-setting decisions require a broad range of evidence from multiple policy dimensions. In this respect, the findings from the three studies provide valuable insights about the financial burden of diseases on households, and the benefit of universal public finance of health policies to mitigate adverse outcomes (e.g. premature deaths), inequalities and financial risks. Specifically, Paper-I has generated evidence on economic burden and CHE associated with seeking HIV and TB services. Papers II and III estimated the magnitude of health and non-health benefits of universal public finance of effective malaria and TB interventions. This section sequentially summarises the key findings of these Papers, the policy implications and discusses these findings with reference to existing literatures. Finally, the strengths and limitations of the studies are discussed.

5.1 Main findings

Paper-I shows the total patient cost of HIV is $ 78 per year and $ 115 per TB episode (where the cost for drug-resistant TB was four times higher). The direct patient costs of HIV and TB care are 69% and 46% of the total costs, respectively. The overall incidence of HIV-related CHE is 20% (i.e. 4% for the richest quintile and 43% for the poorest quintile) and that of TB was 40% (i.e. 20% for the richest quintile and 58% for the poorest quintile). The rate of CHE is higher for patients with TB/HIV co-infection, drug-resistant TB and those who required hospital admission. Financial risk inequality was observed amongst the different income quintiles, with a 15-18 times higher financial burden among poorest relative to the richest.

In Paper-II, a 10% increase in the coverage of the four malaria interventions (ACT, LLIN, IRS and malaria vaccination) through universal public finance averted 358, 188, 107 and 38 premature deaths and 440, 220, 125 and 18 CHE cases per year among malaria at risk population, respectively. ACT and LLIN resulted in a substantial reduction in deaths and case of CHE. The highest health and FRP benefits occurred in the lowest income quintiles. For instance, the poorest two quintiles accounted for almost half of the deaths averted, compared to one-third in the richest two quintiles. ACT, LLIN,

IRS and malaria vaccine were estimated to have an incremental government cost of $ 5.7, 16.5, 32.6, and 5.1 million, respectively.

Paper-III indicates that implementing active case finding from 2018 to 2035 would lead to TB deaths and CHE reductions of 27% and 32%, respectively. Similarly, enhancing DOTS for DS-TB would avert 25% of deaths and 15% of CHE, and improvements in MDR-TB care would avert up to 1% and 6% of deaths and CHE over the same period, respectively. Both the health and financial risk benefits would be greatest for the poorest two quintiles.

5.2 Interpretation and discussion of main findings

5.2.1 Paper-I. Economic burden of HIV and TB

In this study, on average, patients spend $ 78 per year for HIV care and $ 115 per TB episode. Previous studies from Ethiopia also show high OOP spending for HIV and TB care, with a mean cost of $ 141 per year for HIV and $ 177.3 per TB episode (25, 136). These findings also support previous literature in sub-Saharan Africa that found OOP is still the major source of healthcare payment at the point of use, although the direct comparison is challenging as cost measurements differ across the studies (1, 13). This finding would not be unprecedented in view of the greater demand-side financial barriers to accessing healthcare in the country. The 2016/17 Ethiopia Health Accounts (VII) survey report show that OOP spending as a share of total health expenditure is 31% (137). The contribution of OOP is slightly decreasing (i.e. by 6% from 2013/14), but the rate is still very high, given that more than a quarter of the country's population live in poverty (100). Besides, OOP payment for healthcare is inequitable and is deemed regressive by nature, increasing the gap in health outcomes across social groups (138). This study also showed the economic burden of HIV and TB diseases is not homogenous across socioeconomic status, where both diseases represent a disproportionate burden for low-income groups. The relative costs of medical, non-medical and productivity loss in poor households increase their economic vulnerability by consuming a higher proportion of their annual income and savings (11, 136, 139).

This study indicates high level of OOP payment increases the likelihood of CHE in Ethiopia, where 20% of HIV and 40% of TB patients incurred CHE at 10% threshold of annual household income or consumption. This finding supports the results of previous studies from sub-Saharan Africa that documented HIV and TB patient costs are associated with high financial hardship (1, 13). In this study, 7% and 21% of annual household income/consumption is lost due to HIV and TB care, respectively, which is lower than the figures (i.e. 21% for HIV and 30% for TB) reported in previous studies from Ethiopia (25, 136). Consequently, more patients have experienced CHE in the previous studies. Such difference is primarily attributed to the change in the potential coverage of HIV services during the study periods. The previous study was held during the pilot implementation phase of HIV service (i.e. 2005), where the service provision was more centralised. As a result, patients face substantial costs due to delays in seeking care, travelling long distances and being seriously ill, compared to this study, where services are more decentralised and accessible (25). Similarly, the difference with the TB cost is mainly attributable to the expense of nutritional supplements incurred, where the cost is twice the value reported in this study (136). Moreover, more than half of patients with extra-pulmonary TB and MDR-TB had CHE, which was comparable to a study from India that found patients with extra-pulmonary TB encountered twice higher healthcare cost relative to those with pulmonary TB, and the majority of MDR-TB cases also experienced CHE (140).

The proportion of households facing CHE from HIV and TB care varies substantially across different factors, one of which is socio-economic status, where the poorest households suffer the most. This finding confirms many of the studies conducted in sub-Saharan Africa, including Ethiopia (26, 136, 141, 142) that found strong national health financing and social protection schemes are important in responding to the needs of this group. In addition to household socio-economic status, frequent visits to healthcare, hospitalisation episode, TB/HIV co-infection and seeking diagnostic care from private health facilities contribute to heightened vulnerability. This finding is similar to what was previously documented in the systematic review of patient costs in sub-Saharan

Africa where HIV co-infection, type of healthcare provider, and insurance schemes were listed as important determinants of CHE (13, 142).

The finding also indicates that TB/HIV co-infected patients suffer from relatively high healthcare costs and CHE compared to individuals with TB or HIV infections alone, as previously reported (24, 143). The integration of HIV and TB services facilitates the provision of a comprehensive package of service for patients through a one-stop-shop care model (144). However, TB/HIV integration is poorly implemented in several settings. Often the services are either not given at one-location or have strong referral linkages (145). For example, joint TB/HIV collaborative activities have been scaled-up in Ethiopia over the past decades. The TB service deliveries at health facilities is more decentralised than that of HIV services (15). This mismatch contributes to the provision of fragmented services, increases visits to health facilities, and affects the continuity of healthcare, resulting in increased costs of care for households and might even delay access to essential services. Integration could benefit patients more if it is focused on implementation experiences and addresses the prevailing problems of collaborative TB/HIV implementation (e.g. decentralisation of HIV services) in the country.

Another determinant of CHE was the frequency of healthcare visits, which has a positive association with increased patient costs. The decrease in the HIV and TB health facility visits or improved patient scheduling systems has alleviated part of the economic burden and uptake barrier as revealed in previous studies (136, 139). However, if not accompanied by proper support, a decrease in the frequency of visits alone may have implications on retention in care and adherence to treatment with potential consequences on emergence of drug resistance (29). In this context, the community-based systems (i.e. health extension programme) is important for providing both preventive and curative services for vulnerable and rural communities in Ethiopia. The HIV and TB services provision through community-based systems is a cost-effective strategy that improves adherence and FRP in LMICs, including Ethiopia (146, 147). However, according to recent survey, the provision of clinical services such as HIV and TB under the existing health extension programme needs to be strengthened in terms of service delivery (e.g. availability of essential medicines, commodities), trained personnel and infrastructure,

etc. in order to increase the quality of care and meet the growing demand of the population (148).

Insurance scheme enrolment is another determinant of CHE. Despite the comparatively low coverage of health insurance (i.e. 2% for HIV and 6% for TB), scheme members are protected from CHE as opposed to non-members (142, 149). The Government of Ethiopia had introduced a community health insurance system to withstand the economic shocks triggered by healthcare costs through enhancing the systems to pool risks for healthcare costs (13). However, the current coverage is not adequate to attain universal coverage of HIV and TB services and to eliminate the risk of CHE in Ethiopia.

Households have poor resilience to withstand economic shocks and adopt various coping mechanisms in order to limit the economic consequences of healthcare costs. This study shows almost 24% of HIV and 68% of TB participants indicated the use of coping mechanism, from current income and savings, borrowing and selling assets to cover expenses and loss of earnings, although the coping strategies for both diseases were not similar. If these measures are ineffective, households may experience enormous declines in non-health consumptions, such as food, education, and housing, forcing households into poverty. The coping measures are not cost-free, protecting current consumption at the expense of future insecurity or welfare effect. In particular, the use of savings and sale of assets can reduce household economic prospects. Reducing the intake of food or taking children out of school will smooth consumption in the short term, but can adversely affect health and education prospects in the long-term (150). This is a particular concern for African countries where 30% of households cope with healthcare payments through borrowing and selling assets (151).

In Ethiopia, like other African countries, HIV and TB services are exempted from fee at point of care or provided at a subsidised rate in public and private health facilities linked to the national programme, in order to improve equitable access to services and reduce financial risks (13-16). In an environment of “free” provision of HIV and TB services, households continue to face substantial expenses when seeking care. The current free-of-charge programmes for both diseases in Ethiopia are an important milestone on their

own, but do not fully avoid other major healthcare costs (e.g. basic laboratory tests, ancillary medications and hospitalisation, etc.) linked to these services. A high level of payment for HIV and TB care, on the one hand, could lead to CHE and drive households into poverty, and on the other hand, it forces households to make adverse economic choices, such as cutting back on basic necessities including food, shelter and education in order to finance their healthcare (152). Besides costs during treatment phase of HIV and TB services, high pre-treatment cost of HIV and TB services is not only reflected in economic terms, but can also deter or delay families from seeking the needed services (11, 25).

In conclusion, the economic burden of HIV and TB services is context-specific. The difference in service delivery arrangements and health financing mechanisms may affect the populations and breadth of covered services and healthcare costs. While such services were meant to be provided free-of-charge at point of care, the exemptions were not adequate to cover other necessary costs and to provide adequate FRP. The provision of HIV and TB care needs to be person-centred and accompanied by effective diagnosis and community-based approaches to minimise patient non-medical costs. Furthermore, the integration of HIV and TB services with existing prepayment schemes (i.e. national health insurance, tax-based financing, or a mix of this mechanisms) in low-income countries including Ethiopia, helps to reduce patient costs, even though the strength of such systems depends on the socio-economic and political context.

5.2.2 Paper-II. Public financing of malaria interventions

In this study, the ECEA method was employed to evaluate the variation in health gains, private expenditure averted, and FRP across income quintile of universally publicly financed malaria interventions in Ethiopia. Universal public finance at 10% incremental coverage for key malaria interventions could bring major FRP benefits in addition to substantial health gains. This is supported with finding from previous study, where ACT provision for malaria treatment would avert 410 deaths and is comparable with this study's estimates (i.e. 358 deaths averted) using similar incremental coverage (61). However, the extent of malaria-related deaths averted per year with each of the four

interventions fall far below the findings from the universal public finance of pneumonia, diarrhoea prevention and treatment interventions (153, 154). This can be attributed to the rapid decline in the morbidity and mortality of malaria, both globally and in Ethiopia, due to the scale-up of highly effective preventive and curative interventions, compared to other childhood diseases (106). Among the four malaria interventions, ACT and LLIN are the most effective interventions in reducing larger shares of malaria-related deaths and CHE cases per dollar spent. This is consistent with most CEA studies that have shown that malaria interventions, such as ACT and LLIN, are among the best purchases compared to other public health initiatives for malaria control (155). In contrast, the malaria vaccine would prevent the smallest number of deaths (i.e. 38) in children. This finding differs from the prior study of malaria vaccine (i.e. RTS,S vaccine) conducted in Zambia that found a large reduction in deaths and FRP benefits (134). Normalising the result using the same incremental coverage as the Zambia study would avert approximately 257 malaria-related deaths in children in this study (compared to 667). Similarly, standardising income on a monthly basis and adjusting incremental coverage would result in 1,723 cases of CHE averted in this study (compared to 4,411). This difference could be attributed to the high prevalence and deaths from malaria in children, which is 2-5 times higher in Zambia than in Ethiopia (134). Moreover, relative to pneumococcal and rotavirus vaccine, malaria vaccine has low health and FRP impacts, which is largely due to the lower vaccine efficacy (153, 154, 156).

Approximately, one-third of deaths and CHE averted from all malaria interventions occurred in the poorest quintiles, relatively, due to the high burden of malaria among this group. A previous study of childhood pneumococcal vaccines and pneumonia treatment in Ethiopia also confirms the pro-poor distributional benefits, where universal public finance resulted in 30-40% of deaths averted in the poorest quintile. The distributional FRP benefits observed in this study are also consistent with a study held in Zambia, which found that universal public finance of the malaria vaccine provides FRP benefits for the first three income quintiles (134). Furthermore, equity consequences related to the health benefit and FRP of an intervention are a central concern of UHC. Malaria interventions would mainly benefit the poor, given the low health service coverage

among this population. The high prevalence of malaria among the poor contributes to unequal distributional benefits. This indicates that, despite pro-rich malaria intervention coverage, the poorest quintiles accrue higher health benefits. Public financing of malaria interventions enables countries to equitably distribute resources to optimise health outcomes across different subgroups of the population and reduce inequities. Alternatively, it is understood that malaria intervention would widen the existing health inequities if current pro-rich coverage continue.

In this study, the gain in private expenditure averted is evenly distributed across income quintiles, which is inconsistent with results of previous ECEA of childhood pneumonia and diarrhoea prevention and treatment policies, which found the richest would acquire more reduction from private expenditure (153, 154). Unlike previous findings, this study shows that OOP expenses for malaria care do not vary between poor and rich households that neutralise the gain made in private expenditure averted across income groups (153, 154). In addition, malaria preventive measures have resulted in patient cost savings across all income groups, as reported in the previous study (134). However, from the government perspective, a publicly financed malaria policy would increase net costs with little offset from averted malaria-related treatment costs from preventive interventions (134).

In summary, the use of the ECEA method to estimate the impact of the universal public finance of various malaria related interventions could ensure and provide insight whether these interventions reach the intended population and offer the best value for money. The finding illustrated that the universal public finance of malaria interventions were important in improving health and protecting households from the cost of seeking care, particularly the poorest. It is critical for policymakers to consider which malaria interventions provide the greatest protection for families against health loss and financial risks, in addition to targeting the worse off. This would further guide decisions in selecting interventions to be included in the EHSP or HBP.

5.2.3 Paper-III. Impact on health and CHE of expanded TB control

A modelling analysis of expanded TB control interventions was conducted to determine the health benefits and financial risks in terms of reduction in mortality and CHE in Ethiopia from 2018-2035. Although health gain may be the primary value, the assessment of the FRP of TB intervention is another important non-health outcome in places where ill health predisposes households to financial risks (2).

In this study, substantial health and financial burdens were incurred by TB, affecting more than half a million families at baseline (with the existing coverage) during the follow-up period. Implementing active case finding over the period of 18 years would reduce about 206,000 (27% of the baseline) and 193,000 (32%) of TB deaths and cases of CHE, respectively. Similarly, enhancing DOTS for drug-susceptible TB would avert 192,000 (25%) deaths and 93,000 (15%) cases of CHE; and improvements in MDR-TB care would avert up to 6,300 (1%) and 33,000 (6%) of deaths and cases of CHE, respectively. This finding is supported by previous studies in South Africa, where 60,000-240,000 or 5-20% cases of CHE in the base cases were averted by intensified case findings. Similarly, improved DS-TB care would avert approximately 90,000-220,000 or 7-19% cases of CHE, and improved MDR-TB care would avert 70,000-220,000 or 6-18% of baseline CHE cases (157). Hence, improvements in the delivery of core TB interventions through public financing have the potential to reduce the deaths and CHE, thereby enhancing the health and FRP benefits. But the existing passive case finding failed to identify the predicted cases in areas where seeking TB care is poor and would yield substantial benefits through integration with active case finding strategies (158). Furthermore, DOTS is the single global strategy implemented for TB control and has led to a considerable reduction in morbidity and mortality related to TB diseases in endemic countries. Of particular concern, in places with high burden and weak systems, the widespread use of DOTS alone is not enough to rapidly reduce the TB transmission and associated economic consequences in recent years. TB remains a major public health problem in high-burden countries, where a substantial proportion of the population has been latently infected, creating a large reservoir of potential TB reactivation and continued transmission (159). Indeed, DOTs would continue to be the cornerstone of TB

management in high-burden countries like Ethiopia, but complementing with active case finding strategies is an important step towards sustained prevention and elimination of TB diseases (160).

In this study, the universal public financing of TB health policies leads to higher health and FRP benefits for the poorest quintiles. For example, the public financing of active case findings would result in a more than seven-fold reduction in mortality and twelve-fold reduction in CHE for the poorest quintiles compared to the richest quintiles. Similarly, improved implementation of DOTs results in a six-fold decrease in mortality and a fifty-five-fold decrease in CHE among the poorest quintiles compared to the richest quintiles. This finding corroborates with a previous study in India and South Africa, which found that the health and FRP benefits of TB policies were primarily concentrated among the worse-off populations, and none among the richest (70, 157). However, there are still substantial differences between socio-economic groups regarding access to healthcare and the economic burden of TB, indicating the need for policy reinforcement to ensure that all necessary services are given without financial hardship for the worse-off.

Although the health and FRP benefits of the interventions were substantial in absolute terms, most of the baseline deaths and CHE were not eliminated. This finding is supported by previous studies held in India and South Africa, where the reductions in deaths and catastrophic costs would fall below 20% of base-cases (70, 157). The impact would be influenced by the difference in coverage at the baseline level. For example, increasing DOTS coverage for DS-TB has a relatively modest impact as the baseline coverage reported is already high and close to the target to be achieved.

Our finding aids policies and practices, and the public financing of TB interventions such as enhancing active case finding, and improvement in drug-susceptible TB care contributes to a reduction in mortality and CHE, thus improving health and FRP benefits for many patients in Ethiopia. Even if both benefits were high in absolute terms, the reductions in deaths and CHE are still not adequate. Hence, the enhanced implementation of TB prevention and control strategies in Ethiopia alone would not be sufficient to

achieve the target of ending TB and fully prevent CHE over the next decade (i.e. End TB strategy targets). Thus, not only the optimum implementation of available TB initiatives is essential, but also the introduction or expansion of viable social protection measures (e.g. sickness insurance, cash transfers, food assistance etc.) complemented by new diagnostic and treatment technologies are necessary to progress towards the End TB strategy targets in the country.

5.3 Strengths and limitations

In this sub-section, the strengths and limitations of Papers I-III are discussed. In Paper I, primary data sources were used from all (for HIV) and selected regions (for TB) of Ethiopia, and the strengths and limitation of this Paper is discussed separately. In Papers II and III modeling techniques based on large data sources, complemented by assumptions were used, and thus the strengths and limitations of both studies are discussed together.

5.3.1 Validity

5.3.1.1 Internal validity

The internal validity of research refers to the magnitude to which the results reflect the truth in the study population (161). In Paper-I, cost data were collected retrospectively, which may introduce recall bias and influence the outcome of the study. The recall periods tend to vary by types of goods and services consumed, such that a shorter recall period is used for more frequently consumed goods or services such as outpatient services and food items. While a longer recall period is used for goods or services that are consumed less frequently such as non-food items, durable goods, incidents of hospitalisation. Shorter recall periods ease recollection and reduce bias, while longer recall periods are useful to capture several items incurred at different frequencies during the course of illness. However, it is always a challenge to ensure appropriate time to collect cost data in order to minimise recall bias; shorter recall might be affected by over-reporting and assumptions to alleviate the error over the shorter durations, whereas the longer recall period would result less accurate estimates (162). Hence, the period of recall, shorter or longer, depends on the objective of the study and the type of prior event

(162). In this study, the recall period was chosen when participants receiving HIV and TB care had a better recall of their path to care. However, measuring financial burden related to chronic diseases such as HIV and TB through a cross-sectional survey might create uncertainties, even if this study provides an approximation of total cost per patient for a given period (i.e. annual or reported over the disease period). A longitudinal design may overcome these challenges but requires repeated visits and follow-up that entails additional resources, and is therefore beyond the scope of this study. Despite this limitation, the study captures all relevant cost data, including direct and indirect costs, using standard questionnaires. In addition, the cost of HIV and TB care was disaggregated by equity relevant parameters using a relatively larger sample compared to previous studies (1).

There are various measures of living standards and understanding the potential limitations associated with these measures is important. In Paper-I, a direct measure of living standards such as income for HIV and consumption for TB was used. In LMICs, where home production of food is widespread and formal employment is less common, consumption is the preferred living standard measure instead of income (65). In this study, due to unavailability of data related to consumption for HIV participants, income has been used as a proxy of living standards measure. The use of income, unlike consumption, does not allow for the fact that households are able to minimise the variability of health spending overtime through borrowing and saving. Furthermore, it does not take into account home production. However, the majority of the HIV study participants (92%) were from urban areas and formally employed. In addition, data related to the coping mechanisms for HIV care were analysed and reported to minimise income-based limitations. In general, the choice between consumption and income matters more when measuring health inequities. Use of consumption includes borrowing to finance health spending, making these households appear relatively well-off and overstates household's living conditions, whereas income can understate the situation by making a household that is relatively well-off (with regard to consumption) appear to be relatively worse-off (65).

Models of economic evaluation, such as ECEA, have been used in Papers II and III, which require data from a wide range of sources and proxy inputs, as not all parameters are readily available or documented (68, 163). As a result, these national studies sought data from both primary and secondary sources, and uncertainties were inevitable. To acknowledge these effects, a one-way sensitivity analysis in Paper-II and different scenarios in Paper-III were conducted to check the robustness of the model results. In Paper-III, the interventions chosen (Int1 and Int2) were more effective in reducing TB-related deaths and FRP, but the analysis did not include the program costs required to meet the targets. The estimation of these costs, in order to achieve the various levels of coverage across interventions, would better inform the decision on effective allocation of resources. Furthermore, the ECEA approach allows FRP inclusion on economic assessment of health policies that enables selection of interventions for benefit packages based on the extent of how much health and FRP purchased per dollar spent. However, the method does not have decision rules to weigh trade-offs in health benefits, equity and FRP domains that are left to policymakers to carefully assess the trade-offs along with interventions effectiveness and other moral obligations.

Despite these constraints, the studies shed new light by producing data on the magnitude of financial burden, equity consequences and impact of universal public finance policies to protect households from adverse health and non-health consequences (i.e. financial hardship) that might need to be considered by policymakers to tailor suitable policy strategies.

5.3.1.2 External validity

External validity is the extent to which the research finding can be generalisable to the target populations or can be adapted to another context (164). In Paper-I, sampling of HIV survey participants consisted mainly of urban population and the TB survey was conducted in two purposely selected regions, restricting the representativeness of the finding to the whole population, even if probability sampling techniques were employed to recruit the patient samples in the survey. Ideally, the inclusion of both urban and rural populations in the HIV survey and of more geographic locations in the TB survey would

ensure wider representation of the findings. A modeling study, such as ECEA, was used in Papers II and III in order to prioritise TB and malaria policies in Ethiopia. The selection of appropriate policies would be influenced by the results of the model that in turn depend on the accuracy of the input parameters. The input parameters, such as epidemiologic, programmatic, clinical data and unit costs, synthesised in these Papers, were collected from various sources. In fact, local data inputs were used in these studies to minimise bias and ease the extrapolation to other settings (164). But, preferably, the collection and synthesis of such evidence or inputs should be performed in a reasonable manner, eliminating bias and optimising precision in the final result (165). The review of evidence in LMICs, like Ethiopia, is often a challenge due to the limited availability of data and resources. Therefore, such studies may involve the use of available data from both large and small-scale studies complemented by proxy inputs or assumptions that could lead to a trade-off in precision and possible bias (e.g. precise but biased estimation or vice versa). While this is not unprecedented for many economic evaluation studies, it would impact external validity of the findings (164, 165). In Papers II and III, the potential impact of these inputs or assumptions was accounted for by running different scenarios. The modelling used in these papers clearly articulates the intervention and comparators assessed, the perspective of analysis, rely on locally available data, and standard methods that facilitate the generalizability of the findings to other settings with similar characteristics in terms of disease epidemiology or baseline risks, intervention coverage, affordability and health system performance (164).

6 Concluding remarks

In Ethiopia, the economic burden associated with HIV and TB services is enormous, with one-fifth and over one-third (40%) of households incurring CHE, respectively. The service exemption for these diseases was not sufficient to cover other necessary costs and to offer FRP. As a result, households have poor resilience to withstand economic shocks resulting from continuing expenditure on these diseases which jeopardise their welfare.

Health expenditure on HIV and TB care takes a larger share of household income or consumption (7% for HIV and 21% for TB), contributing to CHE and poor health outcomes. Households with comorbidities, complications and repeated healthcare visits are more likely confronted with CHE relative to their counterparts. The healthcare costs caused by these diseases have the potential to divert the consumption of basic goods or be smoothed by the payment from savings, borrowing, and selling asset, which have an adverse effect on household welfare. In addition, spending on HIV and TB care is inequitable, where the poor spend higher proportion of their income/consumption while seeking care and are 15-18 times more likely to suffer from financial hardship. Therefore, targeted efforts to minimise healthcare payments among the poor could be much more affordable than attempts to eliminate all healthcare costs. Ultimately, ensuring that people are protected from the economic effects of these diseases would have to be a key priority of public health policies, in addition to improving the health of the population.

Enhancing the coverage of existing or new strategies for malaria and TB control through universal public finance could save the lives of patients and bring higher FRP benefit, particularly among the poorest segment of the population. The universal public financing of malaria interventions could reduce up to 10% of baseline malaria deaths and CHE cases. Similarly, the universal public finance of TB interventions decreases about one-fourth and one-third of base-case TB-related deaths and CHE cases, respectively. In low-income countries like Ethiopia with severe resource constraints, policies such as ACT and LLINs for malaria, active case finding and DOTS for TB are

the most effective and cheapest ways to improve the lives of the general population, with meaningful benefits for the poorest in Ethiopia. However, the introduction of malaria vaccines alone does not provide substantial benefits, and the impact and feasibility of the vaccines need to be further explored in combination with other measures prior to wider use. Moreover, the substantial health and non-health benefits of publicly financing the interventions would provide policymakers with an important insight for maximising population health and improving equity.

7 Recommendations

Person-centred, effective and focused strategies are essential to fight HIV, TB and malaria in Ethiopia. The availability of preventive and treatment strategies for HIV, TB, and malaria is an opportunity. However, national policies need to recognise the magnitude and distribution of economic consequences in terms of household income loss or reduction of consumption opportunities. Reviewing and expanding the free-of-charge HIV and TB service package to include all the essential diagnostic and treatment services accompanied by the decentralisation of clinical services are therefore critical in reducing the economic burden faced by households.

Furthermore, the high cost associated with HIV and TB care was an indication of a lack of adequate FRP policies, which requires innovative financial and social protection measures. One of the potential strategies for household protection against financial risks was the introduction of prepayments and pooling of funds. Community-based health insurance was scaled-up in the country to improve health service utilisation and ensure financial protections among households in the informal sectors. The development and integration of HIV and TB specific packages into the existing health insurance schemes are useful in ensuring financial protection for households. More importantly, the country needs to take explicit steps to ensure that public spending is a dominant source of health financing. As public spending for health grows, the population has better access to healthcare and FRP that foster the fair realisation of UHC in the country.

In order to move towards equity, appropriate policy solutions that better protect poor households from financial risks should be designed (e.g. targeted approach such as establishing health equity funds for the poor to access full subsidised care or exemption of priority interventions through insurance schemes) (166).

The investment return, in terms of health and FRP, related to the universal public finance of TB and malaria interventions highlights the priority interventions to be financed by the health sector in order to improve the health system performance and the realisation of UHC. Universal public finance allows the country to allocate resources equitably such that the benefits primarily accrue in the poorest quintile, but a strong effort is

required to reach and improve the coverage of high impact interventions among the populations that are relatively poor or most at-risk.

7.1 Future research needs

Cost and cost-effectiveness studies are evolving in LMICs, including Ethiopia, but more studies are required to analyse the health and non-health benefits of health policies to aid priority setting (6).

It is useful to perform a longitudinal study with repeated data collection for chronic diseases such as HIV and TB in order to analyse the recovery mechanisms and the long-term impact of CHE on the socio-economic status of households, workforce engagement and treatment outcomes (6). Measuring the trend of financial hardship and related inequalities, using national data, would help the country to track progress in protecting households against the cost of healthcare (67). In addition, integrating health service measures with financial burden and the worse-off effect would strengthen the economic case for affordable healthcare (6).

Economic barriers are one of the main reasons for low health service coverage in Ethiopia, but other factors, such as geographic barriers, availability of quality services and health infrastructure may play a major role (61, 120). Hence, addressing the economic barriers alone does not guarantee the availability of health services, and future studies could consider other factors that may have an effect on the delivery of health services in the country. In addition, empirical evidence is needed to expand theoretical aspects of the ECEA on how to rank or aggregate the diverse health policy benefits in the areas of health, FRP and equity as well as methods to evaluate multiple equity dimensions at the same time.

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9 Appendices

Papers I-III

Paper I

BMJ Open

Financial burden of HIV and TB among patients in Ethiopia: a cross-sectional survey

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ABSTRACT

Objectives HIV and tuberculosis (TB) are major global health threats and can result in household financial hardships. Here, we aim to estimate the household economic burden and the incidence of catastrophic health expenditures (CHE) incurred by HIV and TB care across income quintiles in Ethiopia.

Design A cross-sectional survey.

Setting 27 health facilities in Afar and Oromia regions for TB, and nationwide household survey for HIV.

Participants A total of 1006 and 787 individuals seeking HIV and TB care were enrolled, respectively.

Outcome measures The economic burden (ie, direct and indirect cost) of HIV and TB care was estimated. In addition, the CHE incidence and intensity were determined using direct costs exceeding 10% of the household income threshold.

Results The mean (SD) age of HIV and TB patient was 40 (10), and 30 (14) years, respectively. The mean (SD) patient cost of HIV was $78 ($170) per year and $115 ($118) per TB episode. Out of the total cost, the direct cost of HIV and TB constituted 69% and 46%, respectively. The mean (SD) indirect cost was $24 ($66) per year for HIV and $63 ($83) per TB episode. The incidence of CHE for HIV was 20%; ranges from 43% in the poorest to 4% in the richest income quintile (p<0.001). Similarly, for TB, the CHE incidence was 40% and ranged between 58% and 20% among the poorest and richest income quintiles, respectively (p<0.001). This figure was higher for drug-resistant TB (62%).

Conclusions HIV and TB are causes of substantial economic burden and CHE, inequitably, affecting those in the poorest income quintile. Broadening the health policies to encompass interventions that reduce the high cost of HIV and TB care, particularly for the poor, is urgently needed.

Strengths and limitations of this study

- ► This study will be of high value to policies aimed at universal health coverage for HIV and tuberculosis (TB) care in Ethiopia due to the financial risk of seeking care.
- ► Patient costs from this study can provide empirical bases for national HIV and TB programmes for adopting public finance or health insurance-based financing strategies.
- ► The patient costs for outpatient and inpatient HIV and TB care are presented together with income and consumption levels of households.
- ► The cost measurements relied on a patient's ability to remember, which increases risk of recall bias.
- ► The HIV sampling consisted primarily of urban population and the TB study was limited to specific regions of the country, therefore, these samples are not necessarily nationally representative.

BACKGROUND

HIV and tuberculosis (TB) are major global health threats that cause a large financial burden on vulnerable populations. Global efforts, in the past two decades, have improved access to lifesaving HIV and TB interventions.[1–3] More than 72 million lives have been saved between 2000 and 2018.[4 5] Nevertheless, high disease burden, inequality in utilisation of healthcare and service quality issues still exist.[1–3] Better understanding of factors that affect use of these services would help countries to achieve universal health coverage (UHC) of HIV and TB services.

The population in need for care is still large. Globally, 1.7 million people acquired HIV infection and 10 million new TB cases occurred in 2018. In the same period, more than 2 million people died from HIV and TB.[4 6] In Ethiopia, the prevalence of HIV among adults was 1% (CI: 0.7% to 1.4%) and the incidence rate of TB was 151/100 000 in 2018.[4 6] In order to end HIV and TB, a comprehensive approach should include medical and non-medical interventions such as socio-economic support and poverty alleviation.[7 8]

Although many countries, including Ethiopia, offer 'free' HIV and TB services, the implemented policies do not adequately provide realistic financial risk protection. The health budget in Ethiopia is low ($33.2 per capita) and 31% of overall health financing is out of pocket payments (OOP).[9 10] Hence, patient and their families, often face both

direct and indirect costs, which create financial burden on households.[11 12] A systematic review showed that individuals in low-income countries spend a mean direct cost of $155 per drug susceptible TB and $406 per drug-resistant TB (DR-TB). The productivity losses were two to three times higher than the direct costs of drug susceptible and resistant cases, respectively.[13] Similarly, for HIV, spending ranges from $95 to $2672 in sub-Saharan Africa.[12] Such high costs are related to catastrophic health expenditure (CHE), which occurs when the OOP exceeds 10% of annual income[14 15] or 40% of household non-food expenditure.[16] In addition, OOP expenses for HIV and TB care may crowd out consumption of basic needs and leave vulnerable households in debt/impoverishment.[12 17 18] Furthermore, high levels of patient cost may affect access to care, and lead to poor treatment outcome and prolonged period with infection.[12 14 19–21]

Many factors may lead to CHE; exemptions of HIV and TB services often applies to limited aspects of the basic care package (eg, CD_4, viral load, acid-fast bacilli and GeneXpert tests), treatment (eg, antiretroviral therapy (ART), anti-TB drugs). Patients pay for prediagnostic services, ancillary medications, some laboratory testing, imaging, adverse event monitoring, hospitalisation, transportation, food, lodging, etc.[19 22–24] In addition, unavailability of diagnostic services in public health facilities pushes patients to seek care from expensive private providers.[22] Furthermore, low health insurance coverage (around 24% as of 2019), and repeated follow-up visits were important contributing financial risk factors.[25 26] It is also imperative that HIV and TB programmes, needs to monitor household protection from CHE (ie, financial risk protection) and its distribution across income groups (equity), as OOP health spending places greater burdens on the poor.[27 28]

In Ethiopia, few studies have been evaluating the extent of patient cost due to seeking HIV and TB care. The costs related to severe forms of the diseases and assessments across income or consumption groups were lacking from the studies reviewed.[22 23 29] Furthermore, none studied predictors of CHE.[22 23 29] Because HIV and TB are chronic diseases and intimately linked, it is reasonable to look at them jointly. This paper aims to estimate the economic burden and incidence of CHE incurred by standard HIV and TB care across income or consumption quintile among Ethiopian households. Moreover, we will assess factors associated with CHE for HIV and TB.

METHODS

Study setting and population

In this study, a nationwide household survey for HIV[10] and a cross-sectional health facility based survey for TB, were used to estimate direct and indirect costs, and CHE.

Data for HIV were collected from mid-September 2016 to mid-October 2016. The total estimated number of people living with HIV (PLHIV) was 722747 in Ethiopia. However, for TB, data were collected from December 2018 to September 2019 in three zones (ie, zone 3 of Afar region, and Jimma and Adama special zones of Oromia region). The three zones were purposely selected and represents 4 million people mirroring the country's geographical and socio-economic heterogeneity. The zones account for 10% and 13% of the TB cases in Oromia and Afar regions (and 6% of the national prevalence), respectively.

Sample size and sampling technique

For HIV, PLHIV associations were used as a sampling frame to select HIV participants, as there is no national registry of PLHIV. The association operates in major cities in all regions and its members were primarily residents in urban areas. The estimated sample size was 4200. The response rate ranges from 92% to 100% across regions. A two-stage stratified cluster-sampling method was employed. In stage one, a sample of 105 HIV associations from a total of 588 were randomly selected and allocated to each region using probability proportional to the size. In stage two, 40 HIV members from each sampled association, in total 4171, were randomly selected and interviewed. Among the study participants (ie, 4171), 1006 had HIV-related care during the data collection period and were considered in our analysis.

For TB, the sample size was calculated using two-population proportion formula with 80% power, 5% type I error, 95% CI and using 39%[21] of households incur CHE among the richest income quartile; and to detect 15% point difference revealed 186 samples for each quartile. The final sample size with 10% non-response rate was 818 (of which 7% were DR-TB). Systematic random sampling was employed to select 27 public health facilities from the three zones. The total sample size was distributed proportional to the TB case load.[30]

Patient and public involvement

The research question of this study is in line with the Ethiopian tuberculosis research plan developed through multiple consultative processes involving broader stakeholders including patient representatives. We plan to disseminate the research findings through the national TB research conferences involving researchers, policymakers, stakeholders and affected communities.

Data collection tools and quality assurance

The data collection was based on a structured questionnaire adapted from the United States Agency for International Development (USAID) for HIV and the World Health Organization (WHO) patient costing tool for TB.[31 32] The questionnaire captures sociodemographic variables, direct cost, indirect cost, productivity loss, assets, income, consumptions and coping-related information. We complemented clinical information for TB through review of medical records.The questionnaire was translated into local languages, pretested and modified accordingly. Trained data collectors under close supervision undertook the face-to-face interview. TB patients

with a minimum of 1 month on treatment were interviewed consecutively and the expenses were reported retrospectively. This schedule of interview is based on WHO's recommendation regarding the cost survey of TB patients.[28 31] Whereas, for HIV, the expenditure in the past 4 weeks for outpatient and 6 months for inpatient care was gathered.

Patient cost

The costs of seeking standard HIV and TB care were estimated from a patient perspective. The expenditure related to routine care, HIV-related opportunistic infection and managing comorbidities was considered for HIV. Likewise, for TB episode, the expenditure in the pathway to care from onset of symptoms, diagnosis and completion of treatment was included.

Direct costs includes household expenditures for medical (ie, registration/consultation fees, laboratory tests, X-ray, medicines, hospital admission) and non-medical services (ie, special food/nutrition, transportation and guardian cost) net of reimbursement. Indirect costs constitute lost income following the disease episode. In order to estimate the indirect cost, patients were asked to estimate the time lost due to receiving and waiting for care, hospitalisation, transportation, lost working days and guardian time (TB). Then the total time lost was multiplied by an hourly wage rate, which was derived from monthly income/consumption by assuming 22 working days a month and 8 hours a day. For children less than 15 years of age, non-medical direct and indirect TB cost was computed for the guardian. Total patient cost is the sum of all direct and indirect costs.

In order to annualise the cost, an average of four HIV outpatient visits and single TB episode outpatient visits was considered. The frequency of outpatient HIV visits per year was extrapolated on the basis of per capita healthcare visits an individual made over the last 1 month among all PLHIV interviewed. This proportion was annualised to an approximately four visits per patient and year. The TB patient cost was extrapolated for the whole duration of TB episode based on an individual data reported retrospectively. All costs were gathered in local currency (Ethiopian Birr) and converted to US dollar ($) with the 2019 exchange rate of $1=29.1468 Ethiopian Birr.[33] For HIV, the cost was first converted to a reference period (2019) using Ethiopia's consumer price index.[34] Due to unavailability of data, we used household income (for HIV) and consumption aggregates (for TB) as a proxy for the household welfare measure and scaled to per adult equivalence (online supplementary appendix 1). In addition, participants were grouped into five-income/consumption quintiles to reflect the socio-economic strata (online supplementary appendix 1).

An incidence of CHE occurs when direct costs (ie, OOP) exceed the 10% threshold of annual household income/consumption.[14 15 17] In addition to the 10% threshold, we carried out further analysis at 20% threshold of both OOP and total cost, and at 40% of non-food expenditure to allow for comparison.[16 21 31 35] Furthermore, the distribution of financial burden (measured as ratio of direct/total costs to total household expenditure) across income quintiles was reported using headcount, overshoot and mean positive overshoot[36] (online supplementary appendix 1).

Data analysis

Data was analysed using Stata V.16 software. The data was summarised using mean with SD or median with IQR due to skewed distribution. The cost was disaggregated by outpatient and inpatient care. A concentration index was used to assess health outcome measure inequality across income quintiles.[36 37] Multivariate logistic regression was conducted to identify determinants of CHE by including significant variables in the univariate analysis. A stepwise regression approach was employed to develop the final model and an adjusted odds ratio (aOR) with 95% CI was reported. P value less than 0.05 declares statistical significance for each test. Multicollinearity was ruled out (variance inflation factor <5). Goodness of fit was checked by Hosmer-Lemeshow test.[38]

Ethical consideration

Informed written consent was obtained from TB participants. Oromia and Afar Regional Health Bureau, and respective zonal health offices provided permission to undertake the TB study.

RESULTS

Out of the total 1006 HIV and 787 TB participants, 75% of HIV and 50% of TB were females (table 1). More than two-thirds of the study participants were in the age group between 25 to 44 years for HIV and 1 to 34 years for TB. The median family size was four (IQR, HIV: 3 to 5, IQR, TB: 3 to 6). The mean (SD) household annual income/consumption per adult equivalence was $1188 ($1288) for HIV and $545 ($462) for TB. Seven per cent of TB patients were co-infected with HIV. Almost all (99%) of HIV and 91% of TB/HIV co-infected study participants were receiving ART. About 22% and 6% of HIV and TB patients had both outpatient and inpatient care, respectively. The mean hospital stay was 11 days for HIV and 10 days for TB. The mean (SD) time interval from first healthcare visit to TB diagnosis (health system delay) was 14 (38) days and 85% of TB were diagnosed in public health facilities.

Patient cost of HIV and TB care

The total mean (SD) patient cost for HIV care was $78 ($170) per year and $115 ($118) for the entire duration of a TB episode (table 2). The mean (SD) direct cost was $54 ($144) for HIV and $53 ($59) for TB, which constitutes 69% and 46% of the total cost, respectively. Medical costs contributed to 68% and 38% of the direct costs for HIV and TB, respectively. Diagnostics and medicine account for 39% of the total HIV cost. The mean (SD)

Table 1 Socio-demographic and clinical characteristics of HIV and TB study participants (Ethiopia)

Background characteristics	HIV (n=1006) N (%)	TB (n=787) N (%)
Gender		
Female	756 (75)	396 (50)
Age in years (mean, SD)	40 (10)	30 (14)
Age group		
<18	–	110 (14)
18–24	14 (1)	190 (24)
25–34	268 (27)	229 (29)
35–44	435 (43)	117 (15)
45–54	202 (20)	86 (11)
55–64	58 (6)	32 (4)
65+	29 (3)	23 (3)
Marital status		
Single	38 (4)	309 (39)
Married/living together	493 (49)	409 (52)
Widowed	277 (27)	24 (3)
Divorced	137 (14)	33 (4)
Separated	61 (6)	11 (2)
Place of residence		
Urban	930 (92)	394 (50)
Rural	76 (8)	393 (50)
Highest level of education		
Illiterate	290 (29)	257 (33)
Elementary	457 (45)	334 (42)
Secondary and higher	259 (26)	195 (25)
Family size		
≤4	640 (64)	443 (56)
>4	366 (36)	344 (44)
Annual household income/consumption		
Lowest	200 (20)	159 (20)
Second	470 (21)	298 (20)
Middle	797 (18)	443 (20)
Fourth	1342 (20)	631 (20)
Highest	3084 (21)	1198 (20)
ART status		
On ART	996 (99)	52 (91)
Not on ART	10 (1)	5 (9)
Past history of illness*		
Yes	1006 (24)	61 (8)
No	3165 (76)	726 (92)
Type of visit		
Outpatient	790 (79)	739 (94)
Inpatient	216 (22)	47 (6)
Number of visits per year/TB episode		
Outpatient	4428 (4 visits/patient)	48 720 (70 visits/patient)†
Inpatient	249 (1 visit/patient)	2409 (73 visits/patient)†
Type of TB		
Pulmonary TB	–	507 (65)
Extra-pulmonary TB	–	222 (28)
Drug-resistant TB	–	57 (7)

*HIV-related comorbidities (HIV), and history of TB (TB).
†The number of total visits per patient reaches 125 for outpatient and 135 for inpatient drug-resistant TB cases.
ART, antiretroviral therapy; TB, tuberculosis.

indirect cost was $24 ($66) for HIV per year, and $63 ($83) per TB episode. The productivity loss related to TB follow-up visits accounts for 36% of the total cost.

The mean (SD) total cost was $63 ($165) for annual outpatient HIV care visit and $110 ($114) for the whole duration of outpatient TB care (table 2). Similarly, the mean (SD) total cost for each hospitalisation was $96 ($139) for HIV and $105 ($78) for TB. For patients having both outpatient and inpatient visits, the mean cost reaches $133 ($178) (p<0.001) for HIV and $ 217 ($157) (p<0.001) for TB.

For TB, the patient costs incurred prior to initiation of treatment are equal to the cost from initiation to completion of TB treatment (paired t-test >0.05). The mean (SD) total cost for those with TB/HIV co-infection reached $188 ($33). Similarly, the total cost of care significantly varies by type of TB, it was $104 ($107) for pulmonary, $140 ($138) for extra-pulmonary and $446 ($732) for DR-TB (Kruskal-Wallis test 41.1, p<0.001) (online supplementary appendix table A1).

Coping costs

HIV and TB care results in adverse financial consequences for households. Nearly 24% of HIV and 68% of TB study participants have adopted coping mechanisms. Nine per cent of HIV and 4% of TB patients have borrowed money; while, 2% of HIV and 19% of TB patients sold their household assets. Furthermore, 12% of HIV patients relied on family assistance and 16% of TB patients used their savings to cope with the costs. Only 2% of HIV and 6% of TB participants are covered by health insurance.

As shown in figure 1, the spikes in the Pen's parade graph revealed that the healthcare costs of HIV and TB cause a large decrease in annual income/consumption for many of the households. The consumption drop for

Table 2 Distribution of household direct, indirect and total cost of HIV and TB care across main cost category in Ethiopia (expressed in $)

	HIV (n=1006)			TB (n=729)		
Cost category ($)	**Outpatient (per year)**	**Inpatient (per single visit)**	**Total**	**Outpatient (per TB episode)**	**Inpatient (per single visit)**	**Total**
(I) Direct medical cost						
Consultation fee						
Mean (SD)	6 (15)	1 (5)	6 (15)	2 (5)	11 (16)	3 (7)
Median (IQR)	0 (0–6)	0 (0–1)	0 (0–5)	1 (0–2)	7 (1–14)	1 (0–2)
Investigation cost						
Mean (SD)	14 (45)	9 (19)	15 (47)	8 (13)	14 (16)	9 (15)
Median (IQR)	0 (0–11)	0 (0–9)	1 (0–12)	4 (0–12)	7 (3–18)	5 (0–13)
Drug cost*						
Mean (SD)	12 (40)	22 (63)	16 (48)	7 (14)	16 (21)	8 (16)
Median (IQR)	0 (0–10)	4 (0–19)	1 (0–13)	1 (0–10)	8 (3–20)	2 (0–10)
Subtotal						
Mean (SD)	32 (88)	32 (77)	37 (98)	17 (24)	40 (37)	20 (30)
Median (IQR)	4 (0–34)	8 (0–32)	6 (0–38)	10 (1–22)	30 (16–45)	11 (1–25)
(II) Direct non-medical cost						
Transportation fee						
Mean (SD)	11 (55)	19 (34)	13 (53)	8 (10)	7 (7)	8 (10)
Median (IQR)	2 (0–8)	6 (0–20)	3 (0–9)	5 (2–11)	7 (3–9)	5 (2–11)
Food/accommodation						
Mean (SD)	3 (50)	10 (30)	5 (48)	23 (29)	28 (34)	25 (31)
Median (IQR)	0	0 (0–5)	0	15 (7–27)	16 (7–38)	16 (7–29)
Subtotal						
Mean (SD)	14 (80)	29 (49)	17 (76)	31 (34)	35 (36)	33 (37)
Median (IQR)	2 (0–8)	10 (0–38)	3 (0–10)	21 (11–38)	20 (9–44)	21 (12–40)
Total direct cost						
Mean (SD)	46 (142)	60 (113)	54 (144)	48 (50)	75 (68)	53 (59)
Median (IQR)	12 (1–45)	22 (4–74)	15 (2–57)	35 (17–61)	54 (26–94)	36 (18–64)
(III) Indirect cost						
Foregone income before treatment†						
Mean (SD)	0	0	0	11 (28)	0	11 (26)
Median (IQR)	0	0	0	0 (0–5)	0	0 (0–3)
Foregone income during treatment						
Mean (SD)	11 (44)	22 (41)	16 (50)	11 (26)	12 (31)	10 (26)
Median (IQR)	0	8 (3–19)	0 (0–8)	0 (0–4)	0	0 (0–3)
Time loss related cost						
Mean (SD)	6 (19)	14 (52)	8 (30)	42 (59)	18 (24)	42 (58)
Median (IQR)	2 (1–4)	2 (1–7)	2 (1–5)	27 (14–49)	8 (5–22)	27 (14–49)
Subtotal						
Mean (SD)	17 (54)	35 (75)	24 (66)	62 (84)	30 (37)	63 (83)
Median (IQR)	3 (1–8)	13 (5–32)	4 (2–17)	36 (17–77)	9 (5–39)	36 (17–78)
(IV) Total cost						
Mean (SD)	63 (165)	96 (139)	78 (170)	110 (114)	105 (78)	115 (118)
Median (IQR)	20 (5–63)	52 (25–109)	27 (7–80)	79 (46–140)	87(39-158)	81 (47–150)

*Drug other than anti-retroviral and anti-TB drugs.
†Not captured in HIV survey.

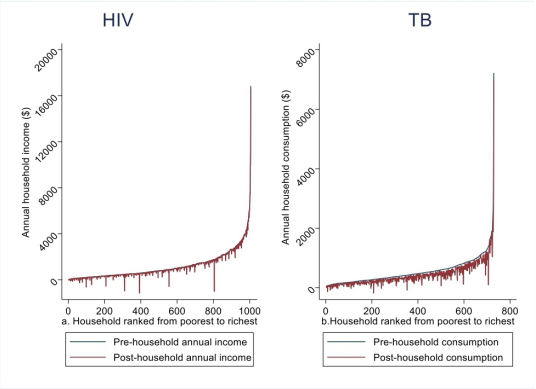

Figure 1 Pen's parade of household annual income/consumption gross and net of payments for HIV (a) and TB care (b) (Ethiopia). TB,tuberculosis.

TB is more pronounced than the income drop for HIV (figure 1).

As shown in table 3, there are inequalities in OOP costs among HIV and TB participants. The total cost rises steadily across the income quintiles and is concentrated among the richer quintiles (ie, the richer the quintile, the higher the cost). From the lowest to the highest income/consumption quintile, the mean (median) total cost of HIV increases from $53 ($20) to $133 ($60), with significant difference among income quintiles (Kruskal-Wallis test 44.7, p<0.001), and for TB the cost increases from $50 ($36) to $202 ($148) (Kruskal-Wallis test 206.5, p<0.001). In general, the median cost (both direct and indirect) seems to be a bit higher for TB patients as compared to that of HIV patients.

Incidence and intensity of CHE

At the 10% threshold, the overall CHE incidence of HIV was 20% (197 households); with 43% of the poorest and 4% of the richest household experiencing CHE (χ^2 for trend −10.58, p<0.001). The incidence is 33% for individuals with inpatient HIV care. The corresponding level of TB was 40% (291 households); with 58% and 20% of the poorest and richest income quintile experienced CHE, respectively (χ^2 for trend −6.79, p<0.001) (table 4). The incidence was much higher for those with TB/HIV co-infection (48%), DR-TB (62%) and was almost universal (94%) for hospitalised TB patients. At the 20% threshold of total expenses, 48% (353 households) of TB households experienced catastrophic total costs (figure 2) (online supplementary appendix table A2).

In our study, for example, the mean overshoot of TB-related CHE was 6.3% (range: 1.9% to 15.3%). On average, households spent 6.3% beyond the 10% threshold for TB care. However, the average positive overshoot among households that experienced CHE was 15.8% (range: 9.2% to 26.6%). Thus, on average, households that experienced CHE spent 25.8% (10% threshold+mean positive overshoot) of their total annual consumption for TB care (figure 2)(online supplementary appendix table A2).

Inequality in financial risk

In addition, as shown in figure 3, inequality in financial risk across income/consumption groups exists. The concentration curves for HIV and TB care costs lie

Table 3 Mean (median) HIV and TB patient costs per year across income quintiles in Ethiopia (expressed in $)

		Cost type					
		Direct		Indirect		Total cost	
Disease category	Income quintiles	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
HIV	Poorest	45 (92)	14 (2–48)	8 (15)	2 (1–7)	53 (97)	20 (3–61)
	Poor	55 (170)	13 (0–52)	10 (19)	3 (1–9)	65 (173)	22 (4–65)
	Middle	50 (118)	19 (3–49)	16 (30)	3 (2–16)	66 (136)	32 (7–65)
	Rich	47 (89)	15 (3–57)	25 (51)	4 (3–20)	71 (111)	27 (7–81)
	Richest	73 (206)	19 (3–79)	60 (124)	14 (5–59)	133 (262)	60 (12–132)
P value*		0.358		<0.001		<0.001	
TB	Poorest	31 (35)	23 (7–41)	19 (20)	11 (6–24)	50 (44)	36 (20–66)
	Poor	44 (48)	27 (15–54)	36 (32)	27 (13–45)	79 (65)	60 (38–96)
	Middle	49 (53)	36 (17–61)	57 (46)	40 (22–82)	106 (79)	82 (57–137)
	Rich	61 (48)	49 (28–84)	79 (63)	58 (27–117)	140 (96)	118 (68–181)
	Richest	78 (86)	54 (34–99)	124 (145)	70 (40–163)	202 (189)	148 (88–260)
P value*		<0.001		<0.001		<0.001	

*Kruskal-Wallis test.
TB, tuberculosis.

Table 4 Multivariate logistic regression model of determinants of CHE for TB and HIV care at a 10% threshold of household income/consumption (Ethiopia)

Variable	aOR (95% CI)	P value
TB		
Frequency of visits*	2.4 (1.9 to 3.1)	<0.001
Hospitalisation		
No	Ref.	
Yes	30.6 (4.8 to 199.8)	0.001
Income quintiles		
Richest	Ref.	
Rich†	4.1 (2.1 to 7.8)	<0.001
Middle	4.9 (2.5 to 9.4)	<0.001
Poor	7.0 (3.6 to13.7)	<0.001
Poorest	14.6 (7.5 to 28.3)	<0.001
Place of diagnosis		
Government	Ref.	
Private	2.6 (1.5 to 4.3)	<0.001
TB/HIV co-infection		
No	Ref.	
Yes	3.2 (1.6 to 6.2)	0.001
Insurance (ie, CBHI)		
Yes	Ref.	
No	2.7 (1.1 to 6.7)	0.038
Type of TB		
Bacteriologically-confirmed TB	Ref.	
Clinically-diagnosed TB	1.6 (1.0 to 2.8)	0.075
Extra-pulmonary TB†	2.6 (1.8 to 4.0)	<0.001
HIV		
Frequency of visits per year*	1.07 (1.003 to 1.1)	0.04
Hospitalisation		
No	Ref.	
Yes	3.3 (2.2 to 4.9)	<0.001
Income quintiles		
Richest	Ref.	
Rich	2.5 (1.1 to 5.8)	0.025
Middle	4.5 (2.1 to 9.8)	<0.001
Poor	9.4 (4.5 to 19.5)	<0.001
Poorest	18.4 (8.9 to 37.7)	<0.001

*Variable treated as continuous.
†Overall test is significant.
aOR, adjusted OR; CBHI, community-based health insurance; CHE, catastrophic health expenditures; TB, tuberculosis.

below the 45° line of equality, which shows a greater concentration of the costs among the rich. However, the financial burden is higher among the poor—the concentration curves for HIV and TB care expenditure in relation to income/consumption lie above the 45° line of equality.

Determinants of CHE

In the multivariate analysis (table 4), three variables were independently associated with HIV related CHE: hospitalised patients (aOR: 3.3, 95% CI: 2.2 to 4.9), being poorest (aOR: 18.4, 95% CI: 8.9 to 37.7) and poor (aOR: 9.4, 95% CI: 4.5 to 19.5) were associated with catastrophic HIV care expenditures. Moreover, every additional visit for HIV care increases the odds of CHE by 7% (aOR: 1.07, 95% CI: 1.003 to 1.1).

Seven variables were significantly associated with TB-related CHE (table 4): private facility diagnosis (aOR: 2.6, 95% CI: 1.52 to 4.33), extra-pulmonary TB (aOR: 2.6, 95% CI: 1.77 to 3.95), hospitalised patients (aOR: 30.6, 95% CI: 4.77 to 199.83), being poorest (aOR: 14.6, 95% CI: 7.49 to 28.26) and TB/HIV co-infection (aOR: 3.2, 95% CI: 1.63 to 6.15) were very likely to have TB-related CHE as compared with their counterparts after adjusting for other variables. Every additional visit for TB diagnosis increases the odds of experiencing CHE by 2.4 times (aOR: 2.4, 95% CI: 1.92 to 3.05). Households with a health insurance scheme have protection from CHE (aOR 2.7; 95% CI 1.06 to 6.73).

DISCUSSION

In this study, we tried to estimate the OOP, total cost, incidence and determinants of CHE among individuals seeking HIV and TB care. This could provide valuable insight into the level of financial risk protection that a health system offers to its population.

HIV care costs and CHE

In Ethiopia, where ART is given free-of-charge, PLHIV had to pay a total of $78 per year for HIV care ($19.5 per visit). The total HIV patient cost was equivalent to 7% of their annual income. As HIV requires lifelong care, such costs have a devastating impact on affected households. Our estimate was lower than the level and rate found in Cameroon 17%,[39] Ethiopia 21%,[23] Nepal 28.5%[40] and South Africa (30%).[41] These variations might arise from different study settings;[39 40] high expenses of additional food and time loss.[41] Similarly, more centralised HIV service delivery, delays in seeking care and long distance travel to access services may explain the difference with the previous study from Ethiopia. Additionally, the annual income in this study was twice that of the latter study.[23] However, a study on outpatient HIV care in Nigeria reported one-fourth of the cost in this study ($21.76).[42]

In our study, the average direct OOP expenditure for HIV care was $54 (ie, 69% of the total cost) and comparable with that of the previous studies from Lao, Ethiopia and Nepal.[19 23 40] Diagnostics, medicines and transportation costs constitute the largest share, and may pose a serious challenge to the success of the HIV programme. This calls for public financing policies (ie, free of charge diagnosis and treatment of HIV-related comorbidities for vulnerable groups) in the next steps of UHC expansion. The productivity loss found here was one-half of

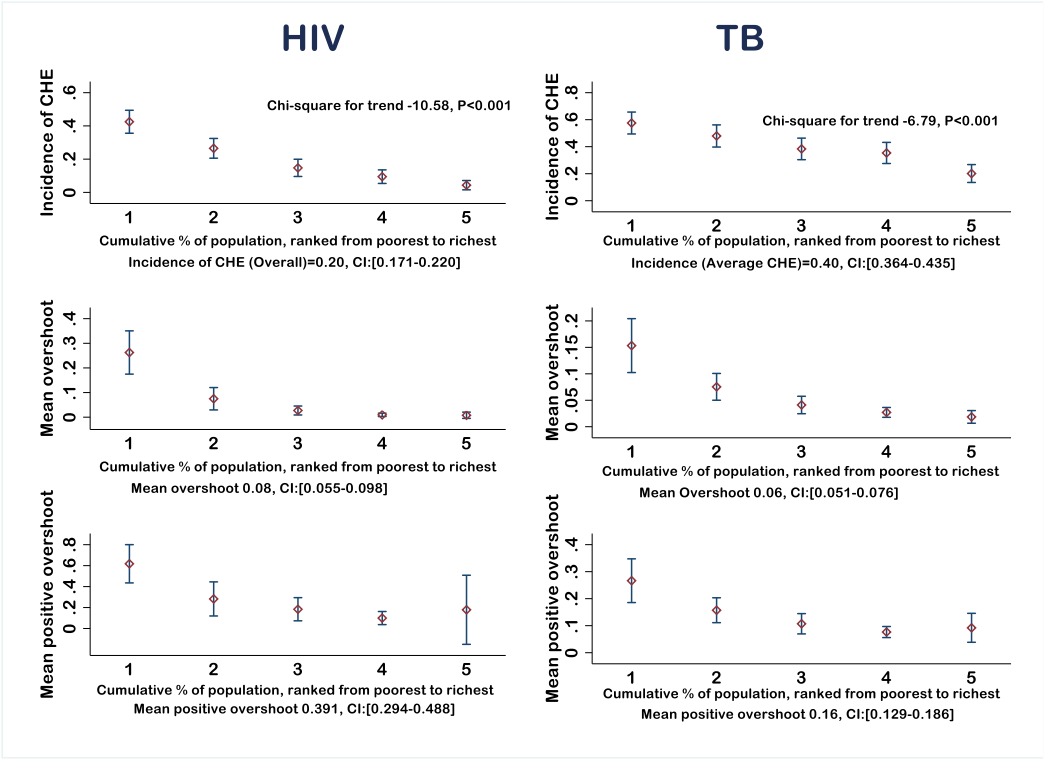

Figure 2 Interval plot (with 95% CI for the mean) of incidence and intensity of HIV and TB-related catastrophic health expenditures (CHE) across income quintiles, using 10% threshold (Ethiopia). CI, confidence interval, TB, tuberculosis.

that of the previous studies in Ethiopia and Nepal,[23 40] but one-fourth of that of Lao study.[19] The difference in productivity losses with previous Ethiopian study could be attributed to a more centralised provision of HIV services and backlog of patients with advanced HIV diseases, unlike this study. The total costs of HIV care increases as income rises. The equity ratios (Q1:Q5, 0.39) showed higher expenditure among the richest income quintile, which is consistent with a study from southeast Nigeria.[43]

In our study, about a fifth (20%) of patients seeking HIV care experienced CHE. A study from India also depicts similar findings.[44] However, the rate is lower than that of a study from Cameroon.[39] Furthermore, the incidence of HIV-related CHE remained relatively high; in particular, where poorest households suffer more. Similar socio-economic inequality was observed in previous studies,[42 43] highlighting the importance of rendering equitable access to all in need of HIV care, particularly for the poor.[39] Consistent with previous studies, being poor is associated with higher CHE.[19 45] In addition, the poor were pushed further beyond the CHE threshold than the better off. This is of great concern, as health shocks are slightly managed by the poor through reduction of basic requirements to compensate for HIV care. Similar to previous studies, being hospitalised was a stronger determinant of CHE.[19 42]

TB care costs and CHE

In our study, patients with TB incurred a total cost of $115 per episode and represents 21% of the annual household income, comparable to a study in South Africa (22%).[46] However, the total cost was less than the figure reported by previous studies in Ethiopia,[22 29] but twice higher than the finding from southern Ethiopia.[47] The variation in cost from previous studies arises from high expenditure on nutritional supplements ($72 vs $25),[29] lower level of

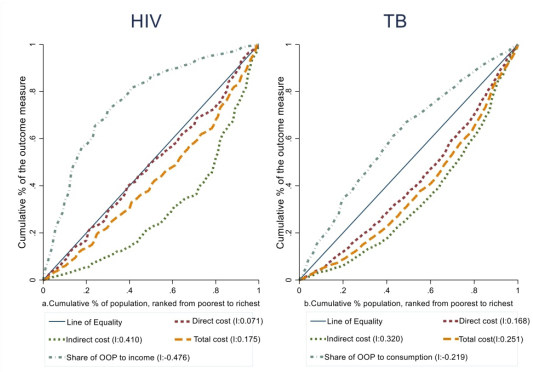

Figure 3 Concentrations curves and index (I) for direct, indirect, total cost and share of OOP to income/consumption for (a) HIV and (b) TB services in Ethiopia. OOP,out-of-pocket payment; TB, tuberculosis.

seeking diagnostic care from public health facilities (64% vs 85%), high rates of clinically diagnosed cases (49% vs 24%), diagnostic delays result in longer losses of working days,[22] only direct cost captured.[47] The average patient costs of DR-TB care were four times higher than drug-susceptible TB care. However, the DR-TB cost was three times lower than findings from another Ethiopian study.[48] Still the devastating nature of DR-TB may put patients at special risk of CHE. The lower costs is mainly due to decentralisation of DR-TB services in recent years and the introduction of shorter multidrug-resistant TB treatment regimen (ie, 71% the study participants took 9-month to 12-month regimen).

In this study, one-half of the mean TB cost was incurred prior to initiation of treatment, which was consistent with many previous studies.[11 21 22 49 50] This is mostly due to payment while demanding for proper diagnosis of TB.[21] In addition to the financial burden of high pretreatment costs, it will be a barrier to complete the diagnostic process, and to timely access treatment and care. These emphasise the need for early case finding with rapid and point of care TB diagnostics, involvement of private care providers and instituting effective referral and linkage.[47]

The direct patient costs incurred constitute 46% of the total, comparable with findings from elsewhere (36%)[51] and systematic review results (40%).[11] However, the proportion was higher than the finding from southwestern Ethiopia (29%) and lower than the report from central Ethiopia (71%).[22 29] Consistent with previous studies, non-medical and indirect costs represent a large share of the TB cost, while medical cost represent less than 20%.[11 22 41] Therefore, ensuring the expansion of TB service package through the effective integration of a health insurance scheme and decentralisation of services can reduce the direct costs.

A higher percentage of households incurs CHE for TB care (40%), which was comparable with studies from Fiji (40%), Ghana (47.6%), China (53%), Philippines (35%) and lower than reported rates from Ethiopia (63%), Nigeria (65%) and Benin (72%).[29 49 50 52–54] However, CHE for TB care was higher in this study compared with findings in studies from India (21%) and Malaysia (6%).[51 55] This variation might arise from cost estimation method, study setting, health system and socio-economic differences. The TB-related CHE was higher than the reported rate for HIV. The main reasons for this are the differences in treatment duration, follow-up frequency and care access between HIV and TB. TB patients experience a very onerous set of direct and indirect costs during diagnostic and intensive phase of directly observed short course therapy (ie, more intense for retreatment, extra-pulmonary and DR-TB cases). After treatment completion and possible sputum conversion, TB patients are less likely to face additional costs. Even though the annual cost of HIV care is lower, PLHIV faces these costs over its lifetime because HIV infection is a chronic disease that needs lifelong treatment. The comparison of incidence and intensity of CHE for TB and HIV is also complicated by the use of income for HIV and consumption for TB-related computations. In developing countries, income is a poor self-reported estimator of welfare due to more common informal employment, seasonal agricultural activities and widespread reluctance to disclose income.[15] Therefore, income could understate the welfare of the household, whereas using consumption may overstate the condition of the household because of the use of dissaving/borrowing to smooth consumption over time.[56]

The mean overshoot for TB was 6.3% and the mean positive overshoot was 15.3%, both were similar with finding from Benin (7.8% and 14.8%) and Nigeria (6.0% and 9.3%).[50 52] TB, inequitably, imposes a greater burden of CHE on the poor households. Even though poor households tend to spend less, a higher share of their income is spent on seeking TB care.[12 29 46 50 52] In addition, the excess CHE beyond the threshold was inequitably high among the poor. This finding is also in line with other studies.[29 50 52] Similar to other studies, hospitalisation, income status and TB/HIV coinfection were among the key determinants of TB-related CHE.[28 49 50 52 55] In addition, even if the health insurance coverage (ie, community-based health insurance) was low and is limited to medical costs, we found protective effect of the scheme against CHE.[57] However, health insurance per se does not alleviate the major TB costs.

Study limitation and strengths

This study has some limitations. First, the cost measurements relied on patient's ability to remember, which increases risk of recall bias. However, we reduced the recall bias by interviewing participants who sought HIV and TB care within the past 1 month, when patients have a better recollection of their pathway to care.[28 31] Second, HIV costs may be overestimated when aggregated over a 1-year period. Third, our findings may not be representative of all patients with TB in Ethiopia, as the study is limited to specific regions of the country. Similarly, the PLHIV associations operate in high HIV prevalence urban areas, where members of these associations may not be representative of both rural and non-members. Moreover, undetected HIV and TB cases not seeking care were not addressed. Despite

these limitations, we used a standard tool and method to conduct the study. We believe that our study will be of high value to inform policy, at national and subnational levels, related to financial risk protection of both diseases, which is central in achieving UHC.

Policy implications

Despite OOP exemption of HIV and TB services in Ethiopia, we found that there is a large gap between the actual level of financial protection provided and the ideal goal. Our findings highlight important policy implications. First, more patient-centred care with effective diagnostics, appointment spacing for stable patients and community-based treatment are required to improve the delivery of HIV and TB services. Second, strategies are required to ensure social and financial risk protection for the households affected by HIV and TB. This requires effective integration of HIV and TB services with social and financial protection schemes, including the provision of travel vouchers, nutritional support and paid sick leaves through multisectoral collaboration.

CONCLUSION

HIV and TB affected individuals and their households in Ethiopia face substantial costs in seeking care despite 'free medical services'. The incidence of CHE related to HIV and TB care was high in all income quintiles, though more so in the poorest households. Policymakers should introduce patient-centred care; expand social and financial risk protection measures to minimise the high patient cost of HIV and TB care, particularly among vulnerable populations.

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Supplementary appendix 1

The financial burden of HIV and TB among patients in Ethiopia: a cross-sectional survey

Lelisa Fekadu[1]*, Eyerusalem Negussie[2], Abdulrahman Jbaily[3], Mieraf Taddesse Tolla[3], Kjell Arne Johansson[1]

S1. Consumption construction

In this study, income (for HIV) and consumption as proxy for income (for tuberculosis) were used as household welfare measure. The consumption aggregates for tuberculosis (TB) was constructed using the overall value of the food (purchased food, home produced food) items, non-food items, and housing information collected at different recall periods (ranging from 1 to 12 months depending on how frequently the item purchased). Then, all reported expenditures on food items, non-food items, and housing were converted to a month period, then added up and multiplied by 12 to create annual consumption for each household.

The income (for HIV) and consumption (for TB) measures were also adjusted for family size and demographic composition to reflect economy of scale. We constructed per adult equivalence through dividing household income/consumption expenditure by an adult equivalent scale. Adult equivalent values (AE) were calculated using $AE = (A + \alpha K)^{\theta}$ for HIV, where A stands for number of adults, K is the number of children in the household, α is the cost of a child relative to an adult (0.33) and θ is the degree of economies of scale (0.9) (1). Whereas for TB, due to the unavailability of child data, we calculated using $AE = hsize^{\beta}$, where "$hsize$" is the actual household size and β was set to be 0.56 (2). Using per adult equivalence income (HIV) and consumption (TB) values, we grouped all households into five income quintiles of equal size.

S2. Incidence and intensity of catastrophic health expenditure (CHE)

S2.1. Measuring incidence of CHE (Headcount)

Catastrophic health expenditure (headcount, H) occurs when household OOP health spending exceeds a predefined threshold (10%) of household income/consumption. Furthermore, we conducted analysis at 20% threshold of both OOP and total cost (new definition of catastrophic cost recommended for TB), and at 40% of non-food expenditure (i.e. net of basic subsistence expenditure).

The CHE headcount is calculated using the equation

$$H = \frac{1}{N}\sum_{i=1}^{N} E_i \,,$$

$$\text{Where,} \quad E_i = 1 \text{ if } \frac{T_i}{X_i} \text{ or } \frac{T_i}{(X_i - FE_i)} > z \text{ and 0 otherwise.}$$

Here, N equals the total sample size, T_i is the OOP health spending of household i, X_i is the total expenditure of household i, FE_i is the food expenditure of household i and z is the specified threshold.

S2.2. Measuring intensity of CHE

The intensity is measured using overshoot (O) and mean positive overshoot (MPO).

S2.2.1. Overshoot

The overshoot measures the extent of average expenditure exceeding the given threshold in the entire sample. The overshoot is calculated using the equation

$$O = \frac{1}{N}\sum_{i=1}^{N} (E_i \left(\frac{Ti}{Xi}\right) - z)$$

S2.2.2. Mean positive overshoot

The mean positive overshoot measures the extent of an average expenditure exceeding the threshold among households experiencing CHE, and is calculated by:

$$MPO = \frac{O}{H}$$

Table A1. Mean (median) patient costs per TB case across three types of TB (Ethiopia) expressed in $.

Income quintiles	Type of TB					
	Pulmonary¥		Extra-pulmonary TB¥		Drug resistant-TB	
	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)	Mean (SD)	Median (IQR)
Poorest	46 (43)	32 (13-62)	60 (45)	46 (32-75)	295 (290)	139 (65-607)
Poor	67 (44)	56 (34-85)	107 (90)	83 (49-136)	159 (85)	153 (68-199)
Middle	102 (80)	75 (48-137)	115 (74)	94 (72-131)	205 (175)	156 (86-250)
Rich	133 (99)	102 (65-176)	155 (86)	133 (79-212)	534 (671)	291 (131-669)
Richest	175 (165)	121 (78-216)	262 (226)	212 (112-294)	971 (1356)	610 (201-821)
Total*	104 (107)	73 (41-135)	140 (138)	96 (58-180)	446 (732)	191 (107-607)

* kruskal wallis test p-value <0.001

¥ CHE at 10% threshold ranged from 33% to 57% for pulmonary and extra-pulmonary TB, respectively.

Table A2. Incidence and intensity of CHE for HIV and TB across different income quintiles and threshold, 2019, Ethiopia

Disease	Measure Of CHE	Threshold	Average	Income Quantile				
				Q1	Q2	Q3	Q4	Q5
HIV	Out-of-pocket HIV spending: as a share of annual income							
	Head count (CHE incidence) %	10%	20	43	27	15	10	4
	Overshoot %	10%	7.6	26.2	7.5	2.7	0.9	0.9
	Mean positive overshoot %	10%	39.1	61.8	28.2	18.3	9.9	17.8
	Out-of-pocket HIV spending: as a share of annual income							
	Head count (CHE incidence) %	20%	11	30	14	6	3	1
	Overshoot %	20%	6.2	22.5	5.6	1.7	0.5	0.6
	Mean positive overshoot %	20%	58.0	74.9	38.6	28.2	18.2	122.0
	Total HIV spending: as a share of annual income							
	Head count (CHE incidence) %	20%	15	38	18	11	6	3
	Overshoot %	20%	7.2	25.4	6.4	2.5	0.8	0.8
	Mean positive overshoot %	20%	48.6	67.8	36.2	23.6	15.0	27.7
	Out-of-pocket HIV spending: as a share of total non-food expenditure							
	Head count (CHE incidence) %	40%	11	31	15	7	3	1
	Overshoot %	40%	13.1	47.4	11.8	3.6	1.0	1.2
	Mean positive overshoot %	40%	116.3	153.0	79.5	55.4	39.7	128
TB	Out-of-pocket TB spending: as a share of annual income							
	Head count (CHE incidence) %	10%	40	58	48	38	35	20
	Overshoot %	10%	6.3	15.8	7.5	4.1	2.7	1.9
	Mean positive overshoot %	10%	15.3	26.6	15.7	10.7	7.6	9.2

	Out-of-pocket TB spending: as a share of annual income							
	Head count (CHE incidence) %	20%	17	38	23	10	8	6
	Overshoot %	20%	3.7	10.7	4.1	1.9	0.7	0.8
	Mean positive overshoot %	20%	21.3	27.8	17.7	18.7	8.8	15.2
	Total TB spending: as a share of annual income							
	Head count (CHE incidence) %	20%	48	60	53	48	46	36
	Overshoot %	20%	10.0	18.6	11.0	8.0	6.7	4.4
	Mean positive overshoot %	20%	20.0	31.1	20.9	16.7	14.7	12.3
	Out-of-pocket HIV spending: as a share of total non-food expenditure							
	Head count (CHE incidence) %	40%	37	50	43	39	33	19
	Overshoot %	40%	29.2	73.0	27.5	18.6	14.9	11.6
	Mean positive overshoot %	40%	78.7	146	63.6	47.7	44.7	59.5
	Where, Q1 = Poorest; Q2 = Poorer; Q3 = Middle; Q4 = Richer; Q5 = Richest.							

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Paper II

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Malaria Journal

RESEARCH

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Health gains and financial risk protection afforded by public financing of selected malaria interventions in Ethiopia: an extended cost-effectiveness analysis

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Abstract

Background: Malaria is a public health burden and a major cause for morbidity and mortality in Ethiopia. Malaria also places a substantial financial burden on families and Ethiopia's national economy. Economic evaluations, with evidence on equity and financial risk protection (FRP), are therefore essential to support decision-making for policy-makers to identify best buys amongst possible malaria interventions. The aim of this study is to estimate the expected health and FRP benefits of universal public financing of key malaria interventions in Ethiopia.

Methods: Using extended cost-effectiveness analysis (ECEA), the potential health and FRP benefits were estimated, and their distributions across socio-economic groups, of publicly financing a 10% coverage increase in artemisinin-based combination therapy (ACT), long-lasting insecticide-treated bed nets (LLIN), indoor residual spraying (IRS), and malaria vaccine (hypothetical).

Results: ACT, LLIN, IRS, and vaccine would avert 358, 188, 107 and 38 deaths, respectively, each year at a net government cost of $5.7, 16.5, 32.6, and 5.1 million, respectively. The annual cost of implementing IRS would be two times higher than that of the LLIN interventions, and would be the main driver of the total costs. The averted deaths would be mainly concentrated in the poorest two income quintiles. The four interventions would eliminate about $4,627,800 of private health expenditures, and the poorest income quintiles would see the greatest FRP benefits. ACT and LLINs would have the largest impact on malaria-related deaths averted and FRP benefits.

Conclusions: ACT, LLIN, IRS, and vaccine interventions would bring large health and financial benefits to the poorest households in Ethiopia.

Keywords: Malaria, Ethiopia, Equity, Financial risk protection, Extended cost-effectiveness analysis

Background

Malaria prevention and control has been prioritized over the past decade in many national health sector plans. As a result, remarkable progress was made worldwide in reducing incidence and mortality from malaria [1, 2]. Due to the expansion of effective strategies, between 2001 and 2013, malaria incidence has dropped by 30% [1, 2]. Despite such progress, malaria remains a major public health burden with a huge impact on the socio-economic

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development of many countries [1, 2]. Nearly one-half of the world population lives in malaria-endemic countries [3]. In 2016 alone, there were an estimated 216 million cases and 445,000 deaths attributable to malaria worldwide [4]. Sub-Saharan Africa accounts for 90% of both cases and deaths due to malaria [4]. Malaria control is unequally distributed across socioeconomic groups and the rates of insecticide- and drug-resistance are increasing. Further scale-up of cost-effective malaria interventions with sustainable financing mechanisms is therefore urgently needed [5].

Ethiopia has made notable progress towards malaria control [6, 7]. Nationally, the prevalence of malaria has declined from 5 to 3% over 2010–2015 [5, 8, 9]. During the same period, malaria-related deaths were reduced by 40% [5]. Scale-up of effective anti-malaria interventions at the primary health care level and improved community engagement were major contributing factors to this progress [10]. There is little evidence from Ethiopia about other factors that might have contributed to malaria decline (e.g. climate change, housing structures and urbanization). However, despite significant progress, much remains to be done in the fight against malaria in Ethiopia, where about 2.6 million cases and 5000 deaths were estimated for the year 2016 [4]. Additionally, the 2015 malaria indicator survey shows that only 40% of the population at risk correctly use insecticide-treated bed nets [9].

Malaria prevention and control are major priorities for Ethiopia's health sector transformation plan (HSTP) [11]. The primary strategies include rolling out long-lasting insecticide-treated bed nets (LLIN) and insecticide residual spray (IRS) for at-risk population [10, 12]. Similarly, artemisinin-based combination therapy (ACT) is recommended as first-line treatment of uncomplicated malaria [10, 12]. Ethiopia has committed to end malaria by 2030 and adopted global malaria control and elimination strategies [12]. As the country moves towards elimination by 2030, tests that are more sensitive will be required to detect subclinical malaria infection to prevent disease transmission [13]. A malaria vaccine (i.e. RTS,S/AS01) could help curb the malaria burden. However, the efficacy of the vaccine is partial and presents rapid waning immunity [14, 15].

Malaria is endemic in many regions of Ethiopia with marked seasonal and geographic variation. Nearly 60% of the total population reside in high-risk areas [10, 12]. In addition to its public health impact, malaria imposes a large financial burden on households, consuming on average 7% of household income [16, 17]. Marginalized and economically vulnerable populations are also at a higher risk of acquiring malaria and of experiencing fatal consequences because of limited health care access and the inability to pay for it [1, 18, 19]. Malaria spending is estimated to cost Ethiopia about $200 million annually or 10% of its total health expenditure [20]. Hence, reducing malaria disease burden has the potential to improve socioeconomic development [21].

The recent attention to universal health coverage (UHC) has provided context to explore mechanisms that would expand access to malaria prevention and treatment services in Ethiopia [22]. This would also help address the high rate (33%) of out-of-pocket (OOP) payments [20]. Given that a quarter of the Ethiopian population lives below the national poverty line [23], OOP malaria treatment costs can be an important barrier to access effective treatment and in pushing households into impoverishment in Ethiopia. Accounting for non-health benefits is essential to reduce health inequalities and contribute to the objectives of UHC [22]. Financial risk protection (FRP) is an important policy objective and can improve access to all needed quality health services without financial hardship [24, 25].

In this paper, the aim is to estimate the potential health, FRP, and equity benefits of universal public finance of scaling up selected malaria prevention and treatment interventions in Ethiopia [26]. This will support policymakers in jointly considering health gains, FRP and equity benefits in resource allocation related decisions.

Methods

Using extended cost-effectiveness analysis (ECEA), we consider the costs and health impact of malaria interventions across population subgroups and estimate the FRP impact on households in Ethiopia [26]. Building on a recent ECEA of malaria vaccine [28], and using a static disease model, are quantified, across socioeconomic groups (i.e. income quintiles), for each of four malaria interventions (ACT, LLIN, IRS, and malaria vaccine): the number of malaria-related deaths and OOP expenditures averted; the corresponding household FRP provided; and the implementation costs. Furthermore, ECEA is also applied across malaria transmission intensities to account for geographic variation of malaria (see Additional file 1: Appendix Table S2).

Malaria interventions

Large scale use of LLINs is a key strategy to reduce malaria burden [29]. A meta-analysis showed that LLIN was effective in both reducing malaria cases (by 50%) and malaria deaths (by 18%) [27]. IRS can eliminate malaria vectors by applying a residual insecticide to the internal walls and ceilings of homes [2, 30], and its use has been shown to decrease plasmodium falciparum malaria by 29% [31]. A complete cure can be expected in 95% of falciparum malaria cases treated with ACT [32]. The

proportion of *Plasmodium falciparum* malaria in Ethiopia totals about 80–90% of all malaria cases [9]. Lastly, a recent clinical trial showed a 26% reduction in the number of episodes and hospital admissions, in children under 2 years of age, following three doses of malaria vaccine (currently under development) [14].

Health benefits

Population at risk of malaria (accounting for 60% of total population—defined as areas with annual incidence > 0 per 1000 population) is the target population for LLIN and IRS (Table 1) [12]. Similarly, the estimated number of annual malaria cases and birth cohorts born in at-risk areas were the target populations for ACT and vaccine, respectively [12, 14]. Target populations were split into income quintiles for LLIN, IRS, and ACT interventions. As for the vaccine, quintile-specific total fertility rates were applied in order to differentiate between the number of susceptible individuals per income quintile (see Additional file 1: Appendix). For each intervention, in order to calculate malaria prevalence by at-risk population per income quintile, first the relative risk of malaria prevalence by income quintile is estimated for the general population [9, 10]. These stratified relative risks were multiplied by average malaria prevalence, in order to split prevalence rates across income quintiles for populations at risk (see Additional file 1: Appendix) [9, 10].

The baseline coverage (before introduction of universal public financing) was 40% for LLIN and 29% for IRS and their respective coverage by income quintile was sourced from the 2016 malaria indicator survey (MIS) (Table 1) [9]. LLIN use, rather than its possession, was selected as a proxy parameter because the actual use of LLIN reflects behavioural change [33]. The percentage for whom care was sought among children who had fever in the past 2 weeks was used as a proxy for probability of seeking malaria care and baseline ACT coverage (35%) [34, 35]. A 10% incremental coverage across quintiles was assumed for each intervention. For the vaccine, in addition to the 10% incremental increase in coverage, a scenario with coverage scale-up from 0 to 33% was also considered (since this is the national coverage level of the basic child immunization programme) [34].

Before intervention, 2.6 million cases and 5000 deaths attributed to malaria were assumed to occur annually in Ethiopia [4]. On average, 1% of all malaria cases would be hospitalized, according to the integrated disease surveillance database [36, 37]. Severe and mild cases were treated as inpatient and outpatient cases, respectively. Deaths averted by each intervention were calculated as a product of disease incidence, case fatality ratio, intervention efficacy and incremental coverage (see Additional file 1: Appendix).

Financial consequences for households

Both inpatient and outpatient care of malaria can impose an economic burden to individual households. Direct medical, non-medical, and indirect costs were extracted from two previously published studies [18, 42]. Before universal public finance (UPF) of each intervention, individuals seeking malaria care would pay about $6 and $66 out-of-pocket (OOP) costs for outpatient and inpatient treatment, respectively [18, 42]. Even if there were no OOP payments for preventive interventions, the three malaria preventive interventions (i.e. LLIN, IRS, vaccine) would lower the risk of malaria and thus household OOP expenditures related to malaria treatment. The amount of OOP expenditures averted per income quintile was quantified, before and after UPF. OOP expenditures averted depended on: target population, incremental coverage, health care use, OOP payments, and preventive intervention effectiveness (see Additional file 1: Appendix).

Financial risk protection benefits

The financial risk faced by households depends on the malaria burden, intervention coverage, and probability of seeking treatment. Annual consumption expenditures were extracted from the Ethiopian Household Income Consumption and Expenditure and Welfare Monitoring Survey as a proxy for income [48]. In this study, a case of catastrophic health expenditures (CHE) was counted when total OOP spending for malaria treatment exceeded 10% of total household consumption expenditures or 40% of capacity to pay (i.e. non-food total household consumption) [49, 50]. UPF introduction would avert a number of CHE cases following the reduction in incidence of OOP expenditures.

Intervention costs

The cost of each intervention was estimated from the health system perspective. Average unit cost estimates for preventive (LLIN, IRS, and vaccine) and curative (ACT) interventions were obtained from published studies (Table 1) [44–47]. The unit cost for LLIN included net price and delivery cost. Similarly, for IRS, insecticide cost accounted for 50%, spray campaign operations and labour for 26%, capital cost for 23% and other commodities accounted for 1% [44, 46, 47]. The average unit cost per fully vaccinated child included vaccine price, and supplies accounted for 84%, and the remaining costs (16%) included training, transportation, waste management [45]. Unit cost of ACT comprised of human resources at 58%, drug and pharmaceutical supplies at 25% and rest was indirect costs [43]. Patient and health system costs

Table 1 Extended cost-effectiveness analysis input parameters for public financing of selected malaria prevention and treatment interventions in Ethiopia

Parameter	Value		References
Epidemiology			
Population at risk of malaria (2016)	61,504,000		[12, 38]
Population for malaria vaccine (2016 birth cohort)	1,984,000		Authors' calculation [34, 38]
Crude birth and child mortality rate, per 1000 population	32, 20		[34]
Total fertility rate, Q_1–Q_5; A[a]	6.4, 5.6, 4.9, 4.3, 2.6; 4.6		[34]
Average household size	4.2		[38]
Number of malaria deaths in the general population, population at risk, and children	5000; 3767; 1790		[4, 39]
Prevalence of malaria in population at risk, Q_1–Q_5; A	4.6; 3.1; 3.6; 2.2; 2.1; 3.1%		[9, 10]
Prevalence of malaria in children, Q_1–Q_5; A	5, 3.3, 2.9, 2, 1.7, 3.1%		[9]
Probability of seeking malaria care, Q_1–Q_5; A	23.8, 30.4, 33.0, 42.3, 50.5; 35.3%		[34]
Case fatality ratio for malaria outpatient and inpatient cases	0.19; 0.65%		[3, 4]
Proportion of malaria-related hospital admissions, Q1–Q5	1.00, 0.90, 0.96, 0.87, 0.83; 0.91%		[36, 37]
Effectiveness of LLIN	50%		[27, 40]
Effectiveness of indoor residual spraying (IRS)	29%		[31]
Vaccine efficacy, Weibull decay after 9 months over 5-years	9–12 months	77%	Authors' calculation based on [41]
	12–24 months	46%	
	24–36 months	23%	
	36–48 months	13%	
	48–60 months	8%	
Effectiveness of artemisinin combination therapy (ACT) on mortality reduction	95%		[32]
Interventions			
LLIN coverage before intervention, Q_1–Q_5, A	26, 36, 42, 47, 44; 40%		[9]
LLIN coverage after intervention, Q_1–Q_5, A	36, 46, 52, 57, 54; 50%		[12] Authors' assumption
IRS coverage before intervention, Q_1–Q_5, A	35, 35, 36, 28, 11; 29%		[9]
IRS coverage after intervention, Q_1–Q_5, A	45, 45, 46, 38, 21; 39%		[12] Authors' assumption
Malaria vaccine coverage before intervention, Q_1–Q_5, A	0		[15]
Malaria vaccine coverage after intervention, Q_1–Q_5, A	10, 10, 10, 10, 10; 10%		Authors' assumption
Malaria vaccine coverage after intervention, Q_1–Q_5, A (fully immunized coverage)	19, 31, 30, 40, 58; 33%		[34]
ACT coverage before intervention, Q_1–Q_5, A	24, 30, 33, 42, 51; 35%		[34]
ACT coverage after intervention, Q_1–Q_5, A	34, 40, 43, 52, 61; 45%		Authors' assumption
Costs (2016 $)			
Out-of-pocket outpatient costs, Q_1–Q_5, A	$6.4, 6.8, 5.5, 6.6, 5.7; 6.2		[42]
Out-of-pocket inpatient costs	$65.9		[18]
Unit cost of malaria treatment outpatient visit	$7.3		[43]
Unit cost of malaria treatment inpatient visit[b]	$31.6		[43]
Unit cost of LLIN	$5.4		[44]
Unit cost per vaccinated child (3 doses)	$26.0		[45]
IRS unit cost per person protected	$5.3		[46, 47]
Household consumption expenditure Q_1–Q_5, A	$227, 369, 499, 671, 1422; 638		[48]
Share of food in total consumption expenditure Q_1–Q_5, A	48, 54, 51, 51, 58, 54%		[23]
GDP per capita 2016	$713		[38]

[a] Q_1 stands for poorest income quintile, Q_5 for richest income quintile, and A for average

[b] Average unit cost estimate for inpatient visit

were extracted from the literature and converted for the year 2016 using Ethiopia's gross domestic product (GDP) deflator [38]. The total costs considered: target population, intervention coverage and intervention unit cost.

Sensitivity analyses

The robustness of the findings were tested by using one-way sensitivity analyses. Specifically, the value of malaria prevalence, case fatality ratio, intervention effectiveness, health services utilization, and intervention unit cost were varied by ± 20%, one at a time, to evaluate the interventions impact on the deaths and CHE averted, across income quintiles.

Results

Deaths and cases of CHE averted by malaria interventions

Increasing coverage (by 10%) of ACT, LLIN, IRS and vaccine among the population at risk would avert 358, 188, 107 and 38 deaths per year in Ethiopia, respectively. The four interventions would also avert 440 (i.e. 10% of the baseline CHE), 220 (5%), 125 (3%) and 18 (2%) CHE cases annually, respectively. Among the interventions, LLIN and ACT would have the largest number of deaths averted and CHE cases averted. In addition, ACT and LLIN would avert $4,277,000 and $214,000 of OOP expenditure, respectively (Table 2).

Distribution of deaths and CHE cases averted by malaria intervention

All four interventions would save larger numbers of lives among the poor, due to the fact that the poor would face a higher malaria prevalence and associated risk factors. For example, ACT would avert twice as many deaths in the poorest income quintile as compared to the richest quintile (Fig. 1). 50% of the deaths averted would be concentrated in the poorest two quintiles. The distribution of deaths averted (by LLIN, IRS and ACT), from poorest to richest quintiles, would be 30, 20, 23, 14 and 13%, respectively. Similarly, the distribution of deaths averted by the malaria vaccine would be 30, 22, 21, 16, and 11%, respectively (Fig. 1).

For each intervention, the gradient in private OOP expenditures averted would be flat across quintiles

Table 2 Total government costs, household out-of-pocket (OOP) expenditures averted, deaths averted, and catastrophic health expenditure (CHE) cases averted from universal public finance of selected malaria interventions at 10% incremental coverage, in Ethiopia

Interventions	Net government costs (2016 USD) (incremental)	OOP expenditures averted (2016 USD)	Deaths averted	Cases of CHE averted
Artemisinin-based combination	5,721,000	4,277,000	358	440
Long-lasting insecticide-treated bed nets	16,489,000	214,000	188	220
Indoor residual spray	32,644,600	122,000	107	125
Malaria vaccine	5,144,000	15,000	38	18

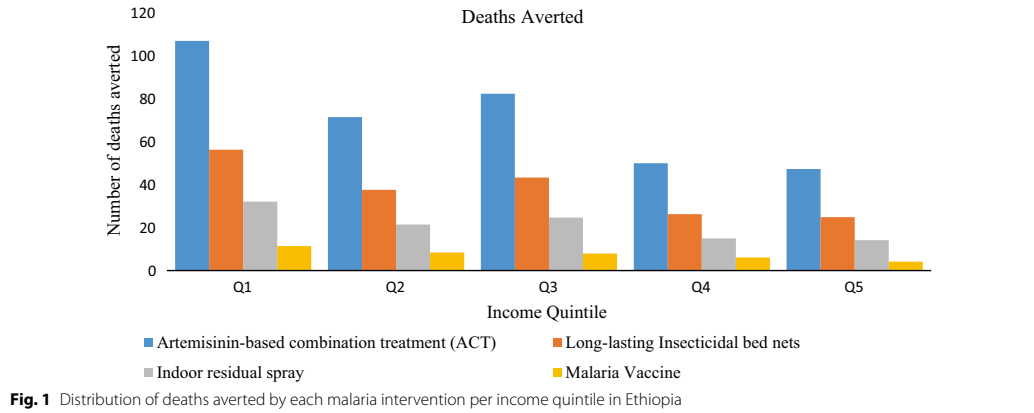

Fig. 1 Distribution of deaths averted by each malaria intervention per income quintile in Ethiopia

as malaria prevalence would decrease with increasing income, but the probability of seeking malaria care would increase as income goes up (Table 3). Therefore, the gains in private expenditures would be evenly distributed across income quintiles. Across the first three income quintiles, a greater number of CHE cases would be averted and the largest benefits would be among the poorest income quintile (Fig. 2).

The annual policy costs of UPF for 10% incremental coverage of ACT, LLIN, IRS and vaccine would be $5.7, 16.5, 32.6, and 5.1 million, respectively. Similarly, due to declines in malaria cases through preventive interventions, $241,000, $137,000 and $16,000 of government expenditures on malaria treatment would be averted annually by LLIN, IRS and malaria vaccine, respectively.

Most of these government savings would be observed within quintile one to three and LLINs would contribute to more than half of these savings. The rollout of malaria vaccines at 10% incremental coverage, under the routine immunization program in the country, would cost around $5 million and avert 38 deaths and reach $17 million and avert about 120 deaths with 33% coverage.

Deaths and cases of CHE averted per million spent

The health benefits per $1 million invested on ACT, LLIN, IRS, and vaccine interventions would be 63, 11, 3, and 7 lives, respectively. Similarly, they would reduce OOP expenditures by $1,560,000, 13,000, 3700 and 2800, respectively; with varying numbers of CHE cases averted by income quintile (see Additional file 1: Appendix, Figs. S1–S3).

Sensitivity analyses

The results of our univariate sensitivity analyses are described in Table 4 (and Additional file 1: Tables S3–S6). Generally, the distribution of health gains is highly prone to variations in malaria prevalence, case fatality ratio and intervention efficacy. The distributions in OOP expenditures averted and CHE cases averted would be more sensitive to malaria prevalence, health care utilization,

Table 3 Out-of-pocket private expenditures averted (in 2016 USD) per income quintile for all malaria interventions in Ethiopia

Interventions	Income group				
	Q1	Q2	Q3	Q4	Q5
Artemisinin-based combination	966,209	847,472	891,970	789,078	782,701
Long-lasting insecticide-treated bed nets	48,310	42,374	44,598	39,454	39,135
Indoor residual spray	27,537	24,153	25,421	22,489	22,307
Malaria vaccine	4879	3659	2556	2278	1215

Q1; poorest quintile, Q5; richest quintile

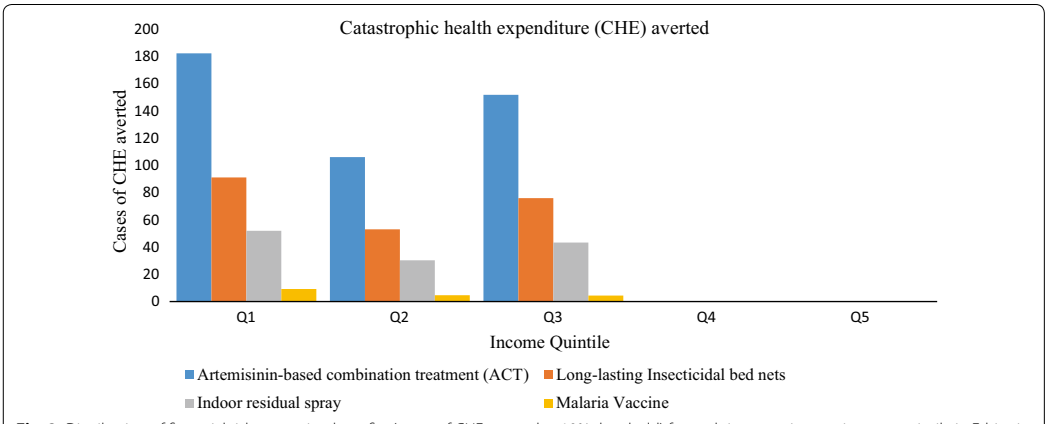

Fig. 2 Distribution of financial risk protection benefits (cases of CHE averted at 10% threshold) for each intervention per income quintile in Ethiopia

Table 4 Sensitivity analyses on the impact on deaths and catastrophic health expenditure (CHE) cases averted when long-lasting insecticide-treated bed nets (LLIN) input parameters vary across income quintiles (Q1 = poorest; Q5 = richest), (low to high shows when input parameters are decreased or increased by 20%, respectively)

Sensitivity analysis LLIN	Q1		Q2		Q3		Q4		Q5	
	Low	High	Low	High	Low	High	Low	High	Low	High
Prevalence of malaria										
Deaths averted	45	68	30	45	35	53	21	32	20	30
Private expenditures averted	38,710	58,070	33,900	58,070	36,090	50,850	31,830	54,130	31,810	47,720
Cases of CHE averted	73	109	42	64	61	92	0	0	0	0
Malaria case fatality ratio										
Deaths averted	46	67	30	45	35	52	21	31	20	30
Private expenditures averted	48,310	48,310	42,370	42,370	44,600	44,600	39,450	39,450	39,135	39,135
Cases of CHE averted	91	91	53	53	76	76	0	0	0	0
Health services utilization										
Deaths averted	56	56	38	38	43	43	26	26	25	25
Private expenditures averted	38,970	58,460	33,450	50,180	35,680	53,520	31,340	47,010	31,620	47,430
Cases of CHE averted	73	110	42	63	61	91	0	0	0	0
Probability of inpatient visit										
Deaths averted	56	57	37	38	43	44	26	26	25	25
Private expenditures averted	47,230	49,390	41,750	43,000	43,680	45,500	39,020	39,890	38,660	39,610
Cases of CHE averted	73	109	42	64	61	91	0	0	0	0
Efficacy										
Deaths averted	45	68	30	45	35	52	21	32	20	30
Private expenditures averted	38,650	57,970	33,900	50,850	35,680	53,520	31,560	47,350	31,310	46,960
Cases of CHE averted	73	109	42	64	61	91	0	0	0	0
Cost inputs										
Government costs	2,625,170	3,963,500	2,632,890	3,971,210	2,621,860	3,960,190	2,634,170	3,972,500	2,628,660	3,966,990
OOP outpatient costs										
Deaths averted	56	56	38	38	43	43	26	26	25	25
Private expenditures averted	39,850	56,770	34,600	50,150	36,680	52,520	32,040	46,860	31,820	46,450
Cases of CHE averted	91	91	53	53	76	76	0	0	0	0

probability of seeking inpatient care, intervention efficacy and OOP expenditures.

Discussion

In this paper, the health and financial benefits of UPF for malaria interventions were estimated across Ethiopian households at all income levels. Overall, all four interventions showed substantial benefits, with ACT and LLIN accounting for the larger shares of malaria-related deaths and CHE cases averted.

All the interventions showed a greater number of deaths averted among the poorest 40% of the population, averted similar OOP expenditures across all income groups, and relatively higher FRP benefits for the poorest 40%. Even if the poor had lower access for care and higher baseline malaria risk, for each of the intervention greater benefits would go toward the poor. This suggests that the malaria interventions analysed in this paper benefit the worse-off and poor populations in remote areas of Ethiopia, who suffer the disease risk at most. Given the relatively lower malaria burden, the four malaria interventions would avert fewer deaths annually, as compared to, other interventions addressing childhood diarrhoea and pneumonia for example [51, 52]. Rapid decline of malaria deaths in Ethiopia over the last two decades and a relatively lower prevalence were the main reasons [6]. Among the four interventions, LLIN and ACT were the two strategies with the highest impact on malaria mortality. In contrast, the malaria vaccine would prevent the smallest number of deaths averted (i.e. 38 per year) as compared to the other interventions. This is largely because the vaccine would be relatively less efficacious [14, 41]: only 2% of malaria-related child deaths would be prevented from the vaccine in this study.

Even though the rich had more access to health services and less malaria burden, the private OOP savings would be similar across all income quintiles. This might be due to the fact that the poor and rich are

spending similar OOP expenditures for malaria care. In absolute terms, the gains in private OOP expenditures could be lower as compared to findings from other Ethiopian ECEAs [51–53]. This might be due to less OOP payments for malaria care as compared to the other diseases. As for the FRP benefits, LLIN and ACT prevented a higher number of CHE cases, and for all interventions, the greatest number of CHE cases averted would occur in the poorest income quintile. In addition, the annual cost of implementing IRS at a 10% incremental coverage for the at-risk population was about $33 million, 2 times higher than that of the LLIN intervention. This corresponds to more than 16% of malaria-related health care spending in Ethiopia [20]. Lastly, though ACT, LLIN, IRS, and malaria vaccine are critical for malaria control and elimination, these interventions would need to be combined with other interventions, such as behavioural change, correct use and implementation, to yield full impact.

Nevertheless, the analysis presented here has several limitations. First, the disease model was static and did not address the dynamics of malaria transmission. Second, because of the unavailability of key input parameters by socioeconomic group, proxy input parameters were used. For example, the percentage who sought treatment for fever in the past 2 weeks was used as a proxy indicator for seeking malaria care. This might have overestimated malaria cases as there are other causes of fever among individuals (besides malaria). The Ethiopian 2016 DHS, the Malaria indicator survey and the ACT malaria consortium guidance on health equity analysis use health care utilisation due to fever in the past 2 weeks as a proxy for seeking care for malaria [9, 34, 35]. Third, due to the lack of disaggregated data, constant rates for case fatality ratio, intervention effectiveness, and inpatient cost inputs were assumed across quintiles. Fourth, unit costs for the vaccine were not specific to Ethiopia. However, despite the limitations, the analysis is crucial as the findings could assist policymakers decide on which health interventions to roll-out to reduce malaria disease burden affecting 60% of the Ethiopian population [9].

The ECEA can also answer some of the equity concerns by providing valuable information on how malaria prevention or treatment strategies would decrease both malaria burden and financial risk incurred by households across various socioeconomic groups in Ethiopia. This study shows that malaria interventions could improve FRP across all income groups, especially among the bottom income groups in Ethiopia. Furthermore, this analysis can help reorienting malaria interventions to target elimination across selected segments of the population, especially among the poor.

Conclusions

All four malaria interventions would save more lives among the poor than among the rich. Preventing and treating malaria provides substantial health benefits and FRP, especially among poor Ethiopians. ACT and LLINs would generate the largest impact on malaria-related deaths averted and FRP benefits. Improving health equity and reducing poverty are major objectives of the Sustainable Development Goals, and the findings of the study presented here would provide insight for policymakers on how to prioritize malaria interventions for targeted population groups including the poorest.

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s12936-020-3103-5.

Additional file 1. Additional Appendix, Figures S1–S3 and Tables S1–S6.

Abbreviations

ACT: artemisinin-based combination therapy; CFR: case fatality ratio; CHE: catastrophic health expenditure; CTP: capacity to pay; ECEA: extended cost-effectiveness analysis; EDHS: Ethiopia Demographic and Health Survey; FRP: financial risk protection; GDP: gross domestic product; IRS: indoor residual spraying; LLIN: long-lasting insecticidal nets; MIS: malaria indicator survey; OOP: out-of-pocket payment; UHC: universal health coverage; UPF: universal public financing; USD: United States dollar; WHO: World Health Organization.

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Authors' contributions

LFA, SV, KAJ, MTT, OFN conceived and designed the study. LFA performed the analysis with input from XJK, DW, LL, SV, KAJ, AJ and MTT. LFA, KAJ, MTT wrote the first draft of the paper, which SV, KAJ, MTT, and AJ subsequently reviewed. All authors provided constructive feedback. All authors read and approved the final manuscript.

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Consent for publication

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Competing interests

The authors declare that they have no competing interests.

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Publisher's Note

Additional appendix

Health gains and financial risk protection afforded by public financing of selected malaria interventions in Ethiopia: an extended cost-effectiveness analysis

By

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1. Introduction

This appendix describes the assumptions underlying the methodology used, and presents supplementary tables, figures, and sensitivity analyses used for the extended cost-effectiveness analysis (ECEA) of universal public finance (UPF) of selected malaria preventive and curative interventions. The methodology for the four malaria interventions is described under section 2 and builds on a previous ECEA of malaria vaccine in Zambia [1].

1.1. Description of model inputs and assumptions for all the interventions

The population at risk of malaria (about 60% of the total Ethiopian population) is the target population for long-lasting insecticide-treated bednets (LLIN) and indoor residual spraying (IRS); for artemisinin combination therapy (ACT), the target population is the estimated number of annual malaria cases of 2016. For malaria vaccine, the target population is the Ethiopian 2016 birth cohort (i.e. calculated as a product of crude birth rate by the size of the at-risk population) in at-risk areas followed over five years to capture the potential full impact of the vaccine. Each target population was evenly distributed across income quintiles for LLIN, IRS and ACT interventions. For the vaccine, quintile-specific total fertility rates were applied in order to differentiate the number of susceptible infants across income quintiles [2].

For each intervention, to distribute the prevalence of malaria for the at-risk population across income quintiles, we used the average malaria prevalence across socioeconomic groups with two diagnostic methods (microscopy and rapid diagnostic test) from the 2015 Malaria Indicator

Survey and the proportion of clinical malaria cases (i.e. 0.5%) from Ethiopia's Federal Ministry of Health (FMOH) malaria review report [3,4].

In order to calculate malaria prevalence by at-risk population per income quintile, we first estimated the relative risk of malaria prevalence by income quintile, and then multiplied it with the prevalence of malaria for the at-risk population. The distribution of malaria cases into outpatient and inpatient categories followed the share of malaria-related hospital admissions and was further disaggregated by income quintile with the distribution of malaria prevalence across income quintiles [5,6].

Case fatality ratios (CFR) for both outpatient and inpatient cases were extracted from the World Health Organization (WHO) 2015 and 2016 malaria reports, which were assumed to be similar across quintiles [7,8]. Then, for all the interventions (except vaccine), we distributed the baseline malaria-related deaths by income quintile through the product of outpatient and inpatient CFR by the number of outpatient and inpatient malaria cases, respectively.

Regarding malaria vaccine, at baseline, among the total malaria deaths, 48% of deaths would occur among under-five children [9]. The total number of malaria deaths was multiplied by this proportion in order to obtain the number of malaria deaths among under-five children [8,9]. Furthermore, malaria deaths were disaggregated by age group, as vaccine efficacy would wane with time since vaccination [8,9]. We used proxy measures (prevalence, treatment coverage, efficacy and child mortality) to distribute the malaria-related deaths by income quintile [10]. We estimated a relative risk ratio of dying from malaria between two income groups *j* and *k* as:

$$\frac{R_j}{R_k} \sim \frac{5q0_j \times (1 - aCOV_j Eff)}{5q0_k \times (1 - aCOV_k Eff)}, \quad (1)$$

where $5q0_j$ is under-five mortality in income quintile j, $aCOV_j$ is malaria treatment coverage in income group j as provided by EDHS 2016 [2], and Eff is treatment effectiveness (assumed constant across quintiles for simplicity) [11]. The risk index in equation (1) (i.e. R_k) is estimated as an average of three proxy measures: probability of being infected with malaria, malaria treatment seeking and a proxy for the relative probability of dying from childhood illness. This approach enables us to distribute the baseline child deaths due to malaria in each quintile. In addition, a Weibull decay function was used to take into account the waning of the vaccine over

the five-year time horizon: $\mathrm{E(t)} = e_0\, exp^{\left(-ln(2)*\frac{(t-to)K}{L^K}\right)}$, where E_0 is initial efficacy against infection (91.1% following third dose), L is half-life protection, K is the decay shape, and $(t - t_0)$ is the time since vaccination [12]. The birth cohort would receive three vaccine doses over 6, 7.5 and 9 months, where vaccine would offer protection starting at age 9 months. UPF would yield a 10% incremental coverage across quintiles for all four interventions.

2. ECEA of malaria interventions

For the three preventive (LLIN, IRS and vaccine) and one curative (ACT) malaria intervention, we divide the population into five income groups j, and we denote y_j the average individual consumption expenditures per income quintile. $p_{in,j}$ denotes the proportion of inpatient malaria cases, and $p_{out,j}$ denotes the proportion of outpatient malaria cases in income quintile j ; and health care utilization is denoted u_j . $OOP_{in,j}$ are the OOP costs of inpatient visit for malaria, and $OOP_{out,j}$ are the OOP costs of outpatient visit for malaria among income group j ; $OOP_{total,j}$ is the total OOP costs in income quintile j. $C_{in,gov,j}$ and $C_{out,gov,j}$ are the government costs for inpatient and outpatient visit for malaria disease treatment in income group j. The intervention has an effectiveness *Eff*; the incremental coverage achieved by the program is Cov_j.

2.1. Estimation of health benefits (i.e. deaths averted)

The number of deaths averted by the intervention in income group j was expressed with a simple static model:

$$D_{av,j} = \left(Eff * Cov_j * D_j\right) \quad , \quad (2)$$

where D_j is the annual number of malaria-related deaths (among under-fives or among all age groups) in income quintile j before the program, and Cov_j is incremental coverage.

2.2. Consequences for household expenditures

We estimated the private expenditures averted in each income quintile j for both preventive interventions (vaccine, LLIN, IRS) and curative interventions (ACT) potentially rolled out in Ethiopia. For preventive interventions, the private expenditures averted by public finance in each income quintile j would be computed as:

$$\mathrm{PE}_{av,j} = Eff * Cov_j * u_j * [\, p_{in,j} * OOP_{in,j} + p_{out,j} * OOP_{out,j}] * n_j \ , \quad (3)$$

where n_j is the annual number of malaria cases (among under-fives or among all age groups) in income quintile *j* before the program.

For curative interventions (i.e. ACT), the private expenditures averted by publicly finance in each income quintile *j* would be computed as:

$$\mathrm{PE}_{av,j} = u_j * [p_{in,j} * OOP_{in,j} + p_{out,j} * OOP_{out,j}] * n_j \quad , \quad (4)$$

where n_j is the annual number of malaria cases (among under-fives or among all age groups) in income quintile *j* before the program, as before-the-program out-of-pocket (OOP) costs are removed by public finance.

2.3. Estimation of financial risk protection benefits

A case of catastrophic health expenditure (CHE) before intervention (CHE_0) is counted when OOP spending for malaria care ($OOP_{in,j}$ or $OOP_{out,j}$ above) is higher than a specified threshold (Th =10%) defined in comparison with consumption expenditures per quintile (i.e. y_j). Then, CHE_0 among those who utilized care occur when $OOP_{in,j}$ or $OOP_{out,j}$ > Th* y_j.

For preventive interventions (vaccine, IRS, LLIN), the introduction of public finance would avert the following number of CHE cases per income quintile *j*:

$$CHE_{av,j} = Cov_j * Eff * CHE_0 \quad . \quad (5)$$

For curative interventions (ACT), the introduction of public finance would avert the following number of CHE cases per income quintile: $Cov_j * CHE_0$.

Cases of CHE were estimated using either a threshold of annual income or a capacity to pay approach (Table S1). For capacity to pay, we extracted the proportion of food expenditure (FE_j) per income quintile *j*. Then, we calculated the absolute value of subsistence expenditure (SE_j) in quintile *j* as $SE_j = (1- FE_j)*y_j$. Capacity to pay was calculated as $y_j - SE_j$ [13,14].

2.4. Quantification of the total costs of the program

From the government perspective, the total costs incurred for the vaccine program are, per income quintile:

$$TC_{Vac,j} = Cov_j * C_{vac} * Popj \quad , \quad (6)$$

where C_{vac} stands for both the costs of the vaccine (3 doses) and program implementation, Cov_j is vaccine coverage per quintile, and $Popj$ is the target population per quintile. The healthcare costs of malaria treatment averted by vaccine for the government (per quintile *j*) are:

$$TC_{HC,j} = Eff * Cov_j * u_j * [(p_{in,j} * C_{in,gov,j} + p_{out,j} * C_{out,gov,j})] * n_j \quad , \qquad (7)$$

where n_j is the annual number of malaria cases (among under-fives or among all age groups) in income group *j* before program. Hence, from the government perspective, the net incremental costs incurred are:

$$TC = TC_{Vac,j} - TC_{HC,prev,j} \quad . \qquad (8)$$

From the government perspective, the total incremental costs incurred for LLIN/IRS program are, per income quintile:

$$TC_{prev,j} = Cov_j * c_{gov} * Popj \quad , \qquad (9)$$

where c_{gov} is the unit costs of LLIN/IRS intervention, $Popj$ is the target population per quintile, and Cov_j is incremental coverage (10%). The total LLIN cost is adjusted by one half, corresponding to one net per two people within a household.

The healthcare costs of malaria treatment averted by LLIN/IRS intervention for the government (per quintile *j*) are:

$$TC_{HC,prev,j} = Eff * Cov_j * u_j * [(p_{in,j} * C_{in,gov,j} + p_{out,j} * C_{out,gov,j})] * n_j \quad , \qquad (10)$$

where n_j is the annual number of malaria cases (among under-fives or among all age groups) in income quintile *j* before program, and Cov_j is incremental coverage (10%). Hence, from the government perspective, the net incremental costs incurred are:

$$TC = TC_{prev,j} - TC_{HC,prev,j} \quad . \qquad (10)$$

From the government perspective, for ACT, the incremental government expenditure per quintile are given by:

$$TC_{cure,j} = Cov_j * n_j * \left(p_{in,j} * C_{in,gov,j} + p_{out,j} * C_{out,gov,j}\right) + \left(p_{in,j} * OOP_{in,j} + p_{out,j} * OOP_{out,j}\right) * u_j * n_j \quad , \qquad (11)$$

where n_j is the annual number of malaria cases (among under-fives or among all age groups) in income quintile *j* before program; u_j is healthcare utilization before program, and Cov_j is the incremental coverage (10%).

3. Additional tables and figures

Table S1. Cases of catastrophic health expenditure averted, for public finance of malaria interventions after a 10% increase in coverage, in Ethiopia.

Interventions	Cases of catastrophic health expenditures averted	Cases of catastrophic health expenditures averted (40% capacity to pay)
Artemisinin-based combination	440	182
Long-lasting insecticide-treated bednets	220	91
Indoor residual spray	125	52
Malaria vaccine	18	9

Annual parasite incidence (API) corresponds to the total number of positive confirmed cases per 1000 population per year [15]. The API level for a specific geographic area is used to classify the districts into control (i.e. API $\geq$ 10), optimization (i.e. 5 < API < 10), pre-elimination and elimination phases (i.e. 0 < API < 5). As shown in Table S2, the health impact of all malaria interventions in the control phase would be substantial, however in other phases selected interventions would yield more benefit.

Table S2: Extended cost-effectiveness analysis results for each intervention per malaria transmission intensity: deaths averted, out-of-pocket (OOP) expenditures averted, and cases of catastrophic health expenditures (CHE) averted.

Intervention	Outcome	0<API< 5 (Pre-elimination /Elimination)	5 ≥ API < 10 (Optimization phase)	API ≥ 10 (Control phase)
LLINs	Deaths averted	4	14	102
	OOP expenditures averted	3,696	16,262	106,213
	Cases of CHE averted	7	20	179
IRS	Deaths averted	2	8	58
	OOP expenditures averted	2,107	9,269	60,541
	Cases of CHE averted	4	11	102
Malaria vaccine	Deaths averted	0	1	10
	OOP expenditures averted	300	1,321	8,627
	Cases of CHE averted	2	10	88
ACT	Deaths averted	8	27	194
	OOP expenditures averted	73,913	325,232	2,124,255
	Cases of CHE averted	13	38	340

Figure S1. Distribution of deaths averted and financial risk protection afforded per US$1 million spent in each income quintile for malaria interventions (Q1 is poorest and Q5 is richest) in Ethiopia.

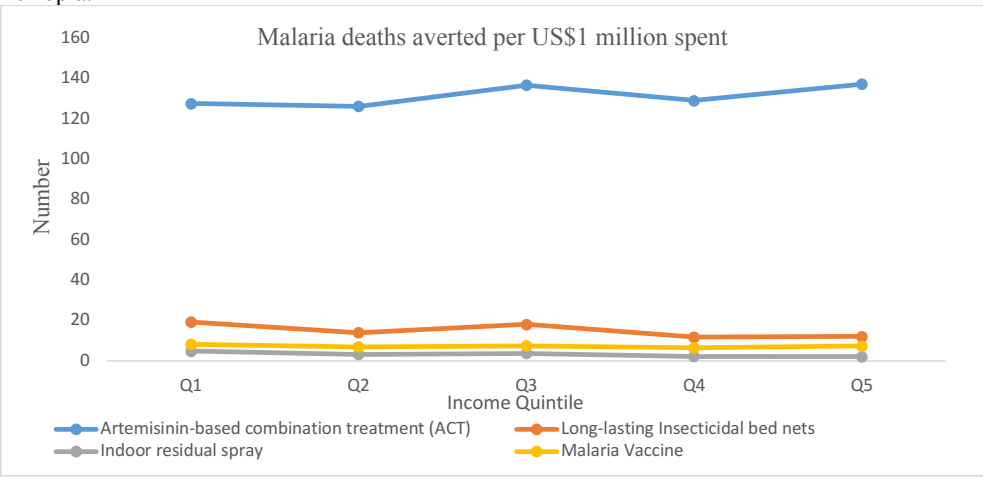


Figure S2. Distribution of financial risk protection afforded per US$1 million government expenditures for each of malaria intervention per income quintile (Q1 is poorest and Q5 is richest) in Ethiopia.

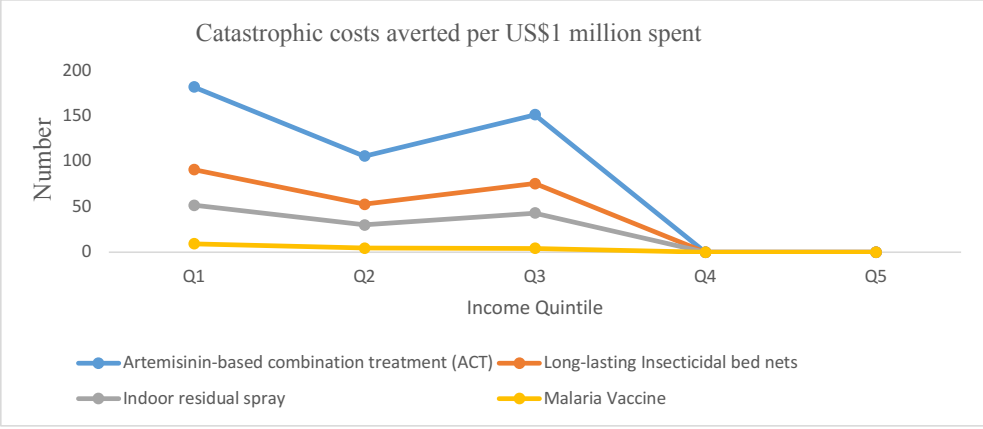
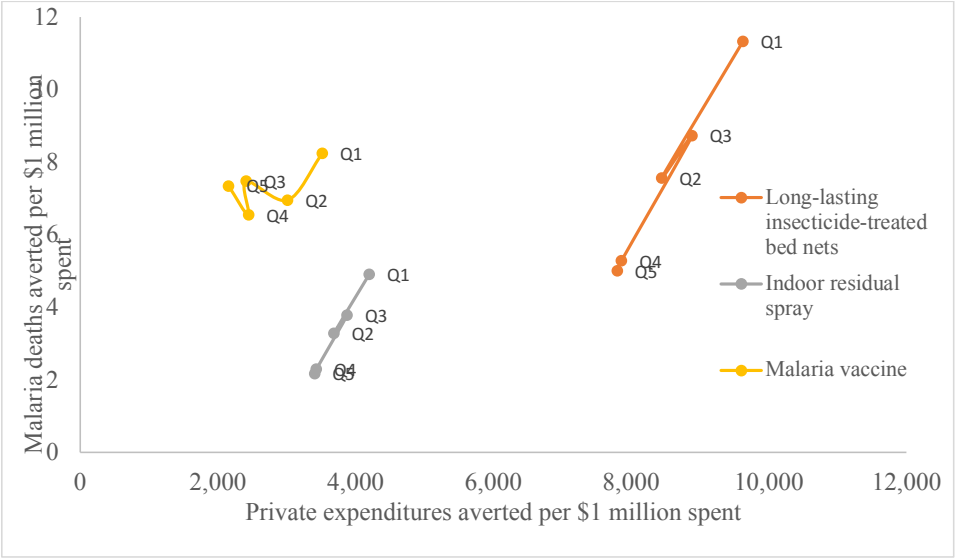
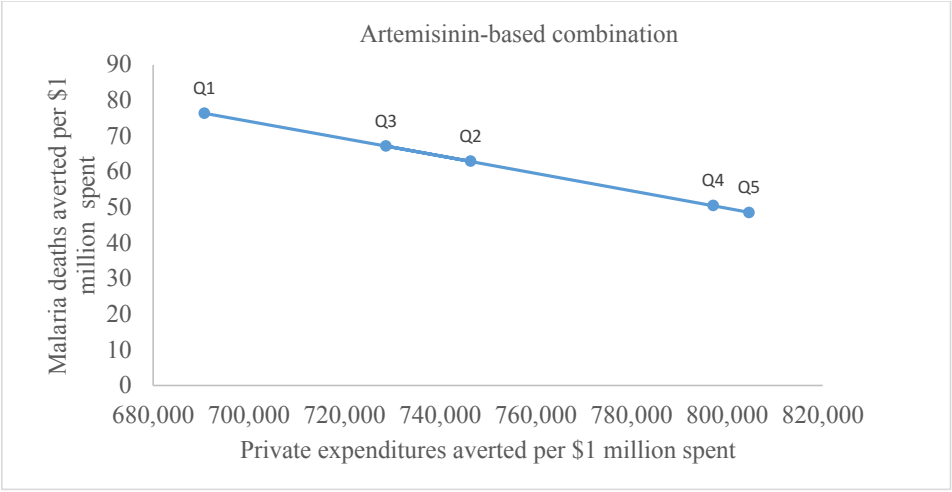


Figure S3. Private expenditure averted (in USD) and malaria deaths averted, per $1 million net government expenditures, per income quintile, by malaria preventive intervention in Ethiopia.

Q1 = Poorest; Q2 = Poorer; Q3 = Middle; Q4 = Richer; Q5 = Richest.





4. Sensitivity analyses

Table S3: Sensitivity analysis of deaths averted and cases of catastrophic health expenditures (CHE) when IRS model input parameters were varied across income quintiles (Q1 = poorest; Q5 = richest), (low to high shows when model input parameters are decreased/increased, respectively).

Sensitivity analysis IRS	**Q1**		**Q2**		**Q3**		**Q4**		**Q5**	
	Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Prevalence of malaria										
Deaths averted	26	39	17	26	20	30	12	18	12	17
Private expenditures averted ($1,000s)	22	33	19	29	21	31	18	27	18	27
CHE cases averted	42	62	24	36	35	52	0	0	0	0
Malaria case fatality ratio										
Death averted	26	38	17	26	20	29	12	18	11	17
Private expenditures averted ($1,000s)	28	28	24	24	25	25	22	22	22	22
CHE cases averted	52	52	30	30	43	43	0	0	0	0
Health care use										
Death averted	32	32	21	21	25	25	15	15	14	14
Private expenditures averted ($1,000s)	22	33	19	29	20	31	18	27	18	27
CHE cases averted	42	63	24	36	35	52	0	0	0	0
Probability of inpatient visit										
Death averted	32	32	21	22	25	25	15	15	14	14
Private expenditures averted ($1,000s)	33	34	28	29	30	31	27	27	27	27
CHE cases averted	50	75	29	43	41	62	0	0	0	0
Efficacy										
Death averted	26	38	17	26	20	30	12	18	11	17
Private expenditures averted ($1,000s)	22	33	19	29	20	31	18	27	18	27
CHE cases averted	42	62	24	36	35	52	0	0	0	0
Cost inputs /IRS										
Government costs for the policy ($1,000s)	5216	7838	5220	7842	5214	7836	5221	7843	5218	7840
OOP outpatient /IRS										
Death averted	32	32	21	21	25	25	15	15	14	14
Private expenditures averted ($1,000s)	23	32	20	29	21	30	19	27	18	26
CHE cases averted	52	52	30	30	43	43	0	0	0	0

Table S4: Sensitivity analysis of deaths averted and cases of catastrophic health expenditures (CHE) averted when malaria vaccine model input parameters were varied across income quintiles (Q1 = poorest; Q5 = richest), (low to high shows when the model input parameters are decreased or increased, respectively).

Sensitivity analysis vaccine	**Q1**		**Q2**		**Q3**		**Q4**		**Q5**	
	Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Prevalence of malaria										
Deaths averted	9	11	7	8	6	8	5	6	3	4
Private expenditures averted	3 900	5 850	2 930	4 390	2 040	3 070	1 820	2 730	972	1 460
CHE cases averted	7	11	4	5	3	5	0	0	0	0
Malaria case fatality ratio										
Deaths averted	9	11	7	8	6	8	5	6	3	4
Private expenditures averted	4 880	4 880	3 660	3 660	2 560	2 560	2 280	2 280	1 210	1 210
CHE cases averted	9	9	5	5	4	4	0	0	0	0
Health care use										
Deaths averted	11	11	8	8	8	8	6	6	4	4
Private expenditures averted	3 940	5 900	2 890	4 330	2 050	3 070	1 810	2 710	981	1 470
CHE cases averted	5	14	2	7	2	7	0	0	0	0
Probability of inpatient visit										
Deaths averted	11	11	8	8	8	8	6	6	4	4
Private expenditures averted	4 770	4 990	3 610	3 710	2 500	2 610	2 250	2 300	1 200	1 230
CHE cases averted	7	11	4	5	3	5	0	0	0	0
Efficacy										
Death averted	9	14	7	10	6	10	5	7	3	5
Private expenditures averted	3 900	5 850	2 930	4 390	2 050	3 070	1 820	2 730	970	1 460
CHE cases averted	7	11	4	5	3	5	0	0	0	0
Cost inputs /vaccine										
Government costs for the policy	1 108 670	1 665 610	970 860	1 458 170	849 670	1 276 070	745 928	1 120 118	451 020	677 275
OOP outpatient /vaccine										
Deaths averted	11	11	8	8	8	8	6	6	4	4
Private expenditures averted	4 020	5 730	2 990	4 330	2 100	3 010	1 850	2 710	990	1 440
CHE cases averted	9	9	5	5	4	4	0	0	0	0

Table S5: Sensitivity analysis of death averted and cases of catastrophic health expenditures (CHE) averted when ACT model input parameters were varied across income quintiles (Q1 = poorest; Q5 = richest), (low to high shows when the model input parameters are decreased or increased, respectively).

Sensitivity analysis ACT	**Q1**		**Q2**		**Q3**		**Q4**		**Q5**	
	Low	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Prevalence of malaria										
Deaths averted	86	128	57	86	67	100	40	60	38	58
Private expenditures averted ($1,000s)	774	1161	678	10167	722	10823	6367	955	6367	954
Cases of CHE averted	146	219	85	127	123	184	0	0	0	0
Malaria case fatality ratio										
Deaths averted	86	127	58	85	66	98	40	60	38	57
Private expenditures averted ($1,000s)	966	966	847	847	892	892	789	789	783	783
Cases CHE averted	182	182	106	106	152	152	0	0	0	0
Health care use										
Deaths averted	107	107	71	71	82	82	50	50	47	47
Private expenditures averted ($1,000s)	779	1169	669	1004	714	1070	627	940	632	949
Cases CHE averted	147	220	84	125	121	182	0	0	0	0
Probability of inpatient visit										
Deaths averted	106	108	71	72	82	83	50	50	47	47
Private expenditures averted ($1,000s)	945	988	835	860	874	910	78	798	773	792
Cases of CHE averted	146	219	85	127	121	182	0	0	0	0
Efficacy										
Deaths averted	86	113	57	75	66	87	40	53	38	50
Private expenditures averted ($1,000s)	966	966	847	847	892	892	789	789	783	783
Cases of CHE averted	182	182	106	106	152	152	0	0	0	0
Cost inputs /ACT/										
Government costs for the treatment (outpatient cost varied) ($1,000s)	1316	1479	1079	1189	1160	1286	950	1028	935	1009
Government costs for the treatment (inpatient cost varied) ($1,000s)	1394	144	1133	1138	1221	1227	989	991	92	974
OOP outpatient /ACT/										
Deaths averted	107	107	71	71	82	82	50	50	47	47
Private expenditures averted ($1,000s)	797	1135	692	1003	734	1050	641	937	636	929
Cases of CHE averted	182	182	106	106	152	152	0	0	0	0

Table S6: Sensitivity analysis of deaths averted when all deaths occurring in the general population is assumed to occur in population at risk (i.e. high case scenario, 5,000 and base case scenario, 3,767) at baseline.

	Intervention	Scenario	Average	Q1	Q2	Q3	Q4	Q5
Sensitivity analysis	ACT	Base case	358	107	71	82	50	47
		High case	475	141	95	109	67	63
	LLIN	Base case	188	56	38	43	26	25
		High case	250	74	50	57	35	33
	IRS	Base case	107	32	21	25	15	14
		High case	143	42	28	33	20	19
	Vaccine	Base case	38	11	8	8	6	4
		High case	51	15	11	11	8	6

As shown in the above table if all malaria related deaths were attributed to population at risk, the death averted proportion would increase by approximately 42% for all interventions.

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Paper III

Ethical Approval

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ቁጥር EPHI 6.13/546
Ref. No
ቀን 05 NOV 2018
Date

Institutional Review Board (EPHI-IRB)

Certificate of Protocol Approval

EPHI-IRB Meeting No. *031*

Protocol number: *EPHI-IRB-121-2018*

Protocol Title: *Patient cost and extended cost effective analysis of communicable Disease (Malaria, HIV/AIDs and TB) interventions in Oromia and Afar Region, Ethiopia*	
Principal Investigator	*Lelisa Fikadu*
Institute	*University of Bergen collaboration with FMoH*
Study site/s	*Oromia and Afar Region, Ethiopia*
Type of Review	✔ Full-Board ☐ *Expedited*
Decision of the meeting	✔ *Approved* ☐ Approved with Recommendation

I. Elements approved-
1. Protocol Version No. *Ver 001*
2. Protocol Version Date: *27 Oct 2018*

II. Obligations of the PI-
1. Should comply with the standard international & national scientific and ethical guidelines
2. All amendments and changes made in protocol and consent form needs IRB approval
3. The PI should report SAE within 10 days of the event
4. End of the study, including technical reports, thesis works and manuscripts should be reported to the IRB

III. Details of recommendation (if approved with recommendation) _____
Institution Review Board (IRB) Approval date: *27 Oct 2018*
Approval period: from *27 Oct 2018* to *26 Oct 2019*
Follow up report expected in: 3 Months _____ *6 Months* ✔ 9 Months_____ One year_____

Chairperson, ~~IRB~~
Signature _____
Date Nov 1, 2018

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The Federal Democratic Republic of Ethiopia Ethiopian Public Health Institute

Director General
Signature _____
Date _____
Ebba Abate (Dr)
Director General

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Camilla Bø Standal	22845821	11.10.2018	2018/1647/REK sør-øst A
			Deres dato:	Deres referanse:
			14.08.2018	

Vår referanse må oppgis ved alle henvendelser

Kjell Arne Johansson
Kalfarveien 31

2018/1647 Helseøkonomisk evaluering i Ethiopia

Vi viser til søknad om forhåndsgodkjenning av ovennevnte forskningsprosjekt. Søknaden ble behandlet av Regional komité for medisinsk og helsefaglig forskningsetikk (REK sør-øst) i møtet 20.09.2018. Vurderingen er gjort med hjemmel i helseforskningsloven § 10.

Forskningsansvarlig: Universitetet i Bergen
Prosjektleder: Kjell Arne Johansson

Project summary (as provided by the Project Manager)

The aim of this study is to assess patient cost, health gain and financial risk protection (FRP) consequences of selected communicable disease (Malaria, HIV/AIDS, and TB) interventions disaggregated by socioeconomic groups in Ethiopia. This study will assess the magnitude and main drivers of patient costs related to Malaria, HIV, and TB in order to guide policies on cost mitigation for reducing financial barriers to access. Provide evidence with equity and FRP to assist policymakers in identifying interventions that represent the best value for money during allocation of resources and health benefits package design. A cross-sectional study design will be used to evaluate the cost of the diseases from the patient perspective. An extended cost-effectiveness analysis will be conducted to estimate the level of malaria, HIV/AIDS, and TB case and deaths averted poverty case or catastrophic case averted per year across income groups at a defined coverage level of the selected interventions.

The Committee's evaluation of the project

The Committee considers that the aim of the project is to assess patient cost, health gain and financial risk protection consequences of selected communicable disease (Malaria, HIV/AIDS, and TB) interventions disaggregated by socioeconomic groups in Ethiopia.

The object of the project is not to generate new knowledge about health, disease, diagnosis or treatment. The project is therefore not considered to be taken in under the substantive scope of the Act on medical and health research (the Health Research Act), jf. § 2. The project may be carried out without an approval from the regional committee for medical and health research ethics in Norway.

Decision

The committee considers the purpose of this study to be outside the remit of the Act on medical and health

research. The project may be initiated without an approval from the regional committee for medical and health research ethics in Norway.

The Committee's decision was unanimous.

It is the responsible institutions' responsibility that the project is carried out with reliability and that local approvals are obtained.

Appeal process

The decision of the Committee may be appealed to the National Committee for Research Ethics in Norway. The appeal will need to be sent to the Regional Committee for Research Ethics, Section A, South East Norway. The deadline for appeal is three weeks from the date on which you receive this letter.

Med vennlig hilsen

Knut Engedal
Professor dr. med.
Leder

Camilla Bø Standal
Seniorrådgiver

Kopi til:kjell.johansson@uib.no; post@uib.no

Questionnaire

Tool to estimate patients' costs

Questionnaire

Questionnaire number: _____

Patient registration number in facility unit TB/MDR TB register : _____

Date of Interview (dd/mm/yy)	Zone	Woreda	Place of interview (Facility name)	Interviewer Name	Supervisor Name
Type of Facility (Circle)	**1. Health Centre** **2. Primary/General/Specialized Hospital** **3. Private Health facility (clinics, hospital)** **4.Other (specify)** _____				

Informed consent:

Good Morning/Good Afternoon. My name is _____. I am working for a research team from University of Bergen, Department of Global Public Health and Primary Care. We are conducting a study on "Cost of tuberculosis to patients and their family during pre-treatment and treatment period". The study would help to estimate the economic cost of tuberculosis at patient and household level, which in turn inform the design of appropriate strategies to address the problem by health policy decision makers both at the local and national level.

It is important for you to understand that your participation in this study is completely voluntary. We would be really grateful if you would agree to participate in this study as your response is very crucial to look at the cost of tuberculosis, but you have full right not to participate in this study. If you decline, there will be no consequence for you and you will receive whatever care and treatment you need at the health facility as usual. And also, there is no payment or reward for your participation in this study.

If you choose to participate in this study you need to know that you may withdraw from the study at any stage without giving any explanation for your withdrawal. We would like to assure you that your personal identifications will not be written on the questionnaire and your answers will be kept confidential. In addition, socio-demographic and clinical information will be gathered from your records and will be kept strictly confidential. At some point I will ask you about your personal income and the income of your household. We will NOT provide this information to any authorities and your response will be kept confidential, also not after the end of the study.

The interview will take 30 minutes.

If you want to ask questions for clarification about the study later on; you can contact Mr. Lelisa Fekadu, by phone numbers 0910-102673 and Dr. Getachew addis, by phone numbers 0944 123110.

Do you want to participate? (Circle) **Yes / No**

If Yes: Thank you! *If No:* Is there a reason why not?

1. *Language* not good enough 2. Time constraint 3. Not comfortable 4. Unspecified

Patient signature_____

Patient Information ***(to be filled in by Interviewer with the help of patient interview and register; fill in also if interview is refused for non-response analysis),*** **(Circle and fill response)**	
1. Gender **1. Male** **2. Female**	
2. Age of the patient: _____ **years**	
3. What is the highest level of education did you complete?	**1. Illiterate** **2. Read and write** **3. Primary** **4. Secondary and above** **5. Diploma/certificate** **6. First degree** **7. Other (specify)**_____
4. Current Marital Status	**1. Single** **2. Married/Living together** **3. Divorced** **4. Separated** **5. Widowed**
5. Occupation	1. Civil Servant 2.Housewife 3. Farmer 4. Laborer 5.Trader/Merchant 6. Housemaid 7. Student 8. No occupation/dependent on household 9. Other (Specify) _____
6. Place of residence	1. Urban 2. Rural 3. Pastoral 4. Other (specify) _____
7. Type of TB or DR TB	1. Pulmonary, bacteriologically confirmed-TB 2. Pulmonary, clinically diagnosed TB 3. Extra-pulmonary TB 4. Pulmonary, bacteriologically confirmed MDR-TB 5. Pulmonary, clinically diagnosed MDR-TB 6. Extra-pulmonary MDR-TB 7. Pre- XDR/XDR TB
8. Date of TB/DR TB diagnosis	(dd/mm/yy) _____/_____/_____
9. Type of bacteriological TB test used for diagnosis and its result	1. Smear microscopy: not done, done-positive, done negative 2. X-pert MTB/RIF: not done, done-positive, done negative 3. Culture: not done, done-positive, done negative
10. Place of TB/DR TB diagnosis	1. Public Hospital 2. Health Center 3. Private hospital/clinic 4. NGO clinic 5. Other (Specify)_____
11. Start date of current TB/DR TB treatment	(dd/mm/yy) _____/_____/_____
12. Currently in intensive or continuation phase?	1. Intensive phase, _____weeks of phase completed

	2. Continuation phase, _____weeks of phase completed
13. Total duration of planned treatment	_____months intensive_____months continuation
14. HIV status **(Only if indicated on register)**	**1. HIV-Positive on ART 2. HIV-Positive not on ART 3. Negative 4. Not tested/Unknown 5. declined**
15. Interviewee	**1. Patient 2. DOT supporter / guardian 3.Other(specify)_____**

NB: If the patient is under 15 years – for children, all questions concerning costs, time spent, income, and income loss before and during TB treatment concern cost for the guardian.

Previous Treatment ***(for TB or DR TB re-treatment cases only)***	
16. a) Have you ever had TB treatment before? ***If No, go to 17.***	**1. Yes (mm/yy treatment ended) _____/_____ 2. No If yes, how many times _____**
b) **If Yes:** Have you completed your last/recent TB treatment?	**1. Yes 2. No**
c) **If No:** why not? **1. Lack of money for treatment costs 2. Drug side effects 3. Moved 4. Distance to facility 5. Other (specify): _____**	
Pre-diagnostic and diagnostic costs	
17. What symptoms did you experience that led you to seek treatment for your current illness? How long did you experience these symptoms before you went to seek treatment? i. Cough 1. Yes _____ day's 2. No ii. Night sweats 1. Yes _____ days 2. No iii. Coughing up blood 1. Yes _____days 2. No iv.Weight loss 1. Yes _____ days 2. No v. Other (specify) 1. Yes _____, _____ days 2. No	
18. Time interval it takes between the date of presentation to a health care provider and the initiation of anti-TB treatment _____ days	
19. Besides yourself, does anyone else of your household receive treatment for TB? ***If yes, fill separate questionnaire for the household member affected with TB at the end.*** [Link the household with this patient questionnaire with similar code]. 1. Yes 2. No	
20. Which of the following types of facilities did you seek care or advice for symptoms of the current illness before TB/DR TB treatment? Check all that apply and Circle first place of visit. 1. Health post ☐ 2. Health Centre ☐ 3. Primary/General/Specialized Hospital ☐ 4. Private Health facility (clinics, hospital) ☐ 5. Pharmacy, drug store ☐ 6. Traditional healer/herbalist ☐ 7. Other (specify) _____	

21. About how much did you spend for each of these visits before you were diagnosed with TB, including the visit when you actually received your diagnosis? *For all that don't apply, mark N/A (not applicable); Fill one line per visit*

Visit: Includes outpatient visits as well as hospitalizations	**Health facility** (copy from question 20 providers where patient sought treatment or advice)	**Travel time to and from health facility** Days: Hours:	**Time spent for visit**** (in Health facility) Days: Hours:	**Administrative Costs** (consultation fee, registration, days charge for hospitalization)	**Lab Test costs** (for sputum, blood or other except x-ray)	**X-ray costs** (includes sending x-ray to radiologist, travel & fees)	**Drug costs** (all kinds total)	**Travel Costs*** (return from health facility, other travel costs)	**Food costs*** *(total)	**Other including Accommodation** (total)	**How did you finance/cover the expenses for these visits** Fill the code from below explanation **(#)** and state the amount). Multiple answers are possible.
1st Visit											
2nd Visit											
3rd Visit											
4th Visit											
5th Visit											
6th Visit											
7th Visit											
8th Visit											
TOTAL											

* If they traveled by private owned vehicle please put the estimated cost of return travel.
**Includes time spent for registration formalities, consultation, laboratory, injections and other time in total.
***Food (any special food bought for example any milk or other food, fluid) bought for the patient in the health facility.
Fill all costs in ETB
1. Current income_____ 2.Own saving_____3.Assets/livestock sale_____4.Borrowed_____5. Insurance (CBHI)_____6. Other(specify) _____

Cost during current TB/MDR-TB treatment

NB: This period for MDR TB starts when the patient is put on effective MDR TB regimen, period before this will be captured on 'Pre-diagnostic and diagnostic Costs' above

22. Where do you take your TB drugs (DOT) and how many times do you go to the health facility for these service per month?
(If the patient has visited two different DOT places, tick the current place and report costs only for that place)

22a) During intensive phase

1. Health center / hospital _____times per month 2. Home

3. Health post _____times per month

4. Work place_____times per month 5. Other_____

If the patient is in intensive phase now and DOT is at home or self-administered, go to 27.

22b) During continuation phase (Please skip to 23 if the patient is currently in intensive phase)

1. Health center / hospital _____times per month 2. Home

3. Health post _____times per month

4. Work place_____times per month 5. Other_____

If the patient is in continuation phase now and DOT is at home or self-administered, go to 27.

23. From your home to the DOT place, how long does it take you to get there (one way)

____ hours walking _____ hours with transport other:_____

24. How long does one of these visits take on average, including time on the road and waiting time (total turnaround time)**?** _____Hours

25. What was the cost of transport (return from health facility, other travel costs) for the last DOT visit, in total for you? _____

26. How much did you spend on food and drinks for the last DOT visit (on the road, while waiting, lunch etc.), in total for you? _____ *If No, go to 27*

Costs related to picking up the TB drugs – where drugs are <u>currently</u> picked up

Filled if household member picks up drugs for either bringing to DOT provider (e.g. family member, DOT at home) or self-administered treatment.

27. How often do you travel to the health facility / health post for picking up your TB drugs?

_____Times / month

28. How long does it take you to get there (one way)

____ hours walking _____ hours with transport other:_____

29. How long does one of these visits take on average, including time on the road and waiting time (total turnaround time)? _____hours

30. What was the cost of transport (return from health facility, other travel costs) last time you picked up drugs, in total for you? _____

31. How much did you spend on food and drinks for last time you picked up drugs (on the road, while waiting, lunch etc.), in total for you? _____ *If No, go to 32.*

32. a) Do you have to pay administration fees when picking up your TB drugs? 1. Yes 2. No

If *No, go to 33.* **b)** If yes, **how much?** _____

Cost related to medical follow-up *(see the doctor or nurse, have tests, check-up, visit for side-effect, doesn't include DOT visits or visits to pick up drugs)*

33. a) Did you ever have to go to the health facility in addition to your regular visits for TB-related medical follow-up visits since the beginning of treatment? *If No, go to 34.*	1. Yes 2. No
b) If yes, how many times have you made visit so far?	_____Times
c) If yes, did you have to pay any additional costs any time during the entire period?	1. Yes 2. No
d) If so, what kind of costs and how much? Administrative fees_____ Sputum test _____ X-ray_____ TB Drugs _____ Other Drugs_____ transport/(return)_____ Other(specify)_____	Total: _____

e) How long does the last medical outpatient visit take on average, including time on the road, waiting time and tests (total turnaround time)? _____Hours

Hospitalization											
34. a) If you are now in the continuation phase, have you been hospitalized during intensive phase?										1. Yes	2. No 3. Not applicable
b) Have you been hospitalized during your current TB treatment? *If No, go to 37.*										1. Yes	2. No
35. If yes: **how many days in total did you stay at the health facility?**										_____ days	
36. About how much money and time did you spend for each of these hospitalizations?											
Hospitalization	**Health facility**	**Travel time to and from health facility** Days: Hours:	**Time spent for visit (in Health facility)** Days: Hours:	**Administrative Costs** (consultation fee, registration, hospital bed)	**Lab Test costs** (for sputum, blood or other except x-ray)	**X-ray costs** (includes sending x-ray to radiologist, travel & fees)	**Drug costs** (all kinds total)	**Travel Costs** (return from health facility, other travel costs)	**Food costs** (total)	**Other including Accommodation** (total)	**How did you finance/cover the expenses for these visits** Circle relevant source(s) and state the amount). Multiple answers are possible.
1st Visit											1.Current income_____ 2.Own saving _____ 3.Assets/livestock sale_____ 4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
2nd Visit											1.Current income_____ 2.Own saving _____ 3.Assets/livestock sale_____ 4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
3rd Visit											1.Current income_____ 2.Own saving _____ 3.Assets/livestock sale_____ 4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
TOTAL											

Guardian Costs	
37. a) Does any family/friend/DOT supporter accompany you on any visits or go in your place (i.e. pre-diagnosis/diagnosis visits, DOT visit, visit to pick up drugs, medical follow-up visits and hospitalization) **to health facility? If No, go to 38.**	1. Yes 2. No
b) If yes, on how many visits has your family/friend/DOT supporter accompanied you or gone in your place? Record pre-diagnosis/diagnosis visits and treatment visits separately Pre-diagnosis/diagnosis costs per visit including hospitalization during this period: Transport _____ Food _____ Accommodation _____ Total pre/diag: _____ Costs during treatment per visit (i.e. treatment visit, medical follow-up visits and hospitalization): Transport _____ Food _____ Accommodation _____ Total Treatm: _____	_____ pre/diag. times _____Treatment times If hospitalized, how many days did he/she stay with you, while in health facility? _____
c) How much does your friend/family/DOT supporter earn per day?	1. _____ 2. Doesn't earn
d) Did anyone in your household drop out of school or interrupt schooling to assist the household because of your TB illness?	1. Yes, _____ persons, Duration of drop out _____ 2. No
e) Does someone stay home specifically to take care of you? If No, go to 38.	1. Yes 2. No
f) If Yes: for how long? _____days	
g) Did they quit their income-earning job to stay home and care for you?	1. Yes 2. No

Other Costs *Food Supplements*	
38. a) Do you buy any supplements for your diet because of the TB illness, for example vitamins, meat, energy drinks, soft drinks, fruits? *If No, go to 39.*	1. Yes 2. No

b) How much did you spend on these items in the last month approximately? _____

Other Illnesses	
39. a) Do you have any chronic illness for which you are receiving treatment? If No, go to 40. **b)** If yes**: which?** _____	1. Yes 2. No
c) Are there any additional costs for you because of this other illness besides the costs that you have already mentioned?	1. Yes 2. No
d) If yes**: How much are these additional costs on average per month?** Tests:_____ Drugs: _____Transport:_____ Food: _____ Other: _____	Total: _____

Coping Costs (filled for DOT, Pick up, medical follow up, guardian, food supplement, other illness section)	
40. How did you finance/cover the expenses for these visits Circle relevant source(s) and state the amount. Multiple answers are possible.	
a) Before TB treatment started? Apply for all patients	1.Current income_____ 2.Own saving (cash or bank deposit) _____ 3.Assets/livestock sale_____ 4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
b) In the intensive treatment phase? Apply for all patients	1.Current income_____ 2. Own saving (cash or bank deposit) _____ 3.Assets/livestock sale_____ 4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
c) In the continuation treatment phase? Apply for patients in continuation phase	1.Current income_____ 2. Own saving (cash or bank deposit) _____ 3.Assets/livestock sale_____

	4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
d) In total *(In case the detail by treatment phase is not available, request the total)*	1.Current income_____ 2. Own saving (cash or bank deposit) _____ 3.Assets/livestock sale_____ 4.Borrowed_____ 5. Insurance (CBHI)_____ 6. Other(specify) _____
41. Has the TB illness affected your social or private life in any way? (More than one answer is allowed)	1. No 2. Food insecurity 3. Divorce or Separated from spouse/partner 4. Loss of Job 5. Social exclusion 6. Other(specify) _____

Household expenditures and income
42. On average how much does your household spend on the following items? a. Food and supplies (e.g. raw ingredients, any semi-cooked/cooked/food/snack/sweets bought, alcohol, cigarette etc.). Per month _____ Raw ingredients :- CEREALS (Enjera (teff), Wheat, Barley, Maize, Sorghum, Millet), TUBERS and STEMS (Potato, Kocho/ Bula), Fruits and Vegetables (including relish and leaves), others (Meat, Milk, Cheese, Eggs, Sugar, Salt, Pasta, Macaroni and Biscuits, Oils/fats/butter) STIMULANTS (Coffee,chat,tea) etc. b. Do you consume any of the home produced food or goods (eg. Teff, wheat, maize, sorgum, fruits, vegetables, milk, milk products etc.) 1. Yes 2. No If yes, specify _____ c. If you were to buy the same food from the market, how much would it cost on an average per month? _____ d. Utilities (electricity, water, telephone (both landline and mobile) Per month _____ e. House/land/shop rent per month: _____ f. Soup/OMO, firewood, candles, charcoal, kerosene per month. _____ g. Education (School for children or self) per term (3 months) _____ h. Health care (for the household) per term (3 months) _____ i. Clothes/shoes per year _____ j. Transport cost per month _____ k. Goods and utensils (kitchen equipment (cooking pots, linens (sheets, towels, blankets) furniture etc.) household use. Per year _____

l. Replacements of household appliances (stove, inverter, fridge, food processor, lanterns, fuel and maintenance of car etc.) Per year _____
m. Other cost per year (describe e.g. contributions, Edir, recreations) _____

43. How much do you estimate was the average income of your household per month BEFORE the TB illness?

1. Income patient: _____ 2. Income of head household _____ 3. Income of household _____
4. Welfare payments and government assistance _____ 5. Other:_____ 6.Total: _____

44. How much do you estimate is the average income of your household per month NOW?

1. Income patient: _____2. Income of head household _____ 3. Income of household _____
4. Welfare payments and government assistance _____ 5. Other:_____ 6.Total: _____

45. a) Do you have any other source of income [house rent, shop, restaurants, dairy, agriculture, rental from agricultural land and animals, car, money sent from relative etc?]

1. Yes 2. No

45b) If yes, what is the six month average income from these sources _____

46. a) Do you receive per month in allowances or gratuities, cash transfer including in-kind payments such as uniform, housing, food item, and transport that were not included in the salary you just reported?

1. Yes 2. No

46b) If yes, what is the average allowance from these sources per month _____?

47. Approximately how many working days of income have you lost due to your TB illness overall?

_____working days before diagnosis of TB (but due to TB disease)

_____working days after TB diagnosis

48. Asset and socio-economic indicators

A1) What are the main walls made of in the dwelling where your household lives?

1. No walls 2. Bamboo/wood with mud 3. Cement
4. Corrugated iron 5. Other (Specify) _____

A2) What is the main material of the roof in the dwelling where your household lives?

1. Thatch/leaf 2. Rustic Mat/Plastic Sheets 3. Corrugated Iron
4. Cement/Concrete 5. Other (Specify) _____

A3) What is the main material of the floor in the dwelling where your household lives?

1. mud/dung 2. Bamboo/reed 3. Wood planks 4. Cement
5. Ceramic 6. Brick tiles 5. Other (Specify) _____

A4) How many rooms are there in your dwelling? _____ Number of rooms used for

Sleeping? _____

A5) Family size _____

A6) Does this household own any livestock or poultry? 1. Yes 2. No

A7) If yes to A6, how many of the following are owned by the household

Number of Goats _____Sheep _____milk cow, oxen, bulls _____

Donkey/Horse/Mule_____Camel _____ Chicken or Poultry _____ Other(specify)_____

A8) What kind of toilet does most members of your household use?

1. Flush toilet 2. Improved pit latrine 3. Public toilet 4. Open field
5. Not improved toilet 6. Neighbours' 7. Other (Specify)_____

A9) What kind of fuel does your household usually use for cooking? (More than one response is possible)

1. Electricity 2. Animal dung 3. Bio-gas 4. Kerosene 5.Wood
6. Coal, lignite, peat 7. Charcoal 8. Other (specify)_____

A10) Ask the availability of the following assets

1. Is there a radio in the household?	1. Yes	2. No
2. Is there a bicycle in the household?	1. Yes	2. No
3. Is there a motorbike in the household?	1. Yes	2. No
4. Is there a car or mini-truck/bajaj in the household?	1. Yes	2. No
5. Is there a cell phone in the household?	1. Yes	2. No
6. Do you have landline telephone in household?	1. Yes	2. No
7. Is there a refrigerator in the household?	1. Yes	2. No
8. Is there a television in the household?	1. Yes	2. No
9. Is there electricity in the household?	1. Yes	2. No
10. Is there a table in the household?	1. Yes	2. No
11. Is there a chair in the household?	1. Yes	2. No
12. Is there a bed in the household?	1. Yes	2. No

A11) What is the main source of water for drinking for your household?

1. Pipeline 2. Public 3. Protected well 4. Unprotected well
5. River 6. Spring protected 7. Unprotected spring 8. Other (specify) _____

A12) Does any member of household own any agriculture land? 1. Yes 2. No

If Yes how many hectares do you own? _____

49. If the government could provide you with some service to ease the burden of TB on you and your household, what would you prefer to have? ***State options, choose one***

1. Transport vouchers 2. Food vouchers 3. More efficient service

4. Other (specify): _____

We would like to know the cost of the TB illness on the welfare of your household; that is, we would like to put a value on the TB illness which includes pain and suffering.

Therefore, we would like to know how much it would be worth to you if you could avoid becoming ill with TB in the first place. Note that we don't ask what you actually can, but what you would be willing pay if you had an unlimited amount of money.

50. How much would you be willing to pay for not becoming ill with TB in the first place?
1. Under 500 2. Between 500 and 1000 3. Over 1000 4. Other (specify) _____

51. What if the price you had to pay to avoid or prevent TB in the first place is higher than the amount you have said above, will you be willing to pay? 1. Yes 2. No

52. What if the price you had to pay to avoid or prevent TB in the first place is lower than the amount you have said above, will you be willing to pay? 1. Yes 2. No

53. Say, if due to inflation or an unforeseen economic situation, the price for TB services increased tremendously, what is the maximum amount you are very certain to pay bearing in mind your average monthly income. _____

54. If you are not willing to pay any amount at all, what might be the possible reasons?

1. Do not believe my TB is curable.
2. Do not have money
3. Do not like the TB services
4. My health is not getting any better

Thank you for your cooperation! Is there anything you would like to ask or say?

Date, Signature by Interviewer: _____, _____

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