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Distributional cost-effectiveness analysis in low- and middle-income countries: illustrative example of rotavirus vaccination in Ethiopia

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2-4 key messages: detailing concisely the main points of the paper

- Policy makers in low- and middle-income countries on the path to universal health coverage face hard choices about which services to prioritise and how to scale up delivery
- These choices can involve equity trade-offs between improving total health and reducing social inequalities in health
- We show how such equity trade-offs can be quantified, and how policy makers can use this information to make transparent decisions, using the example of rotavirus vaccination in Ethiopia
- We do this using a new method called distributional cost-effectiveness analysis, which we adapt for use in low- and middle-income country settings

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Abstract

Reducing health inequality is a major policy concern for low- and middle-income countries (LMICs) on the path to universal health coverage. However, health inequality impacts are rarely quantified in cost-effectiveness analyses of health programmes. Distributional cost-effectiveness analysis (DCEA) is a method developed to analyse the expected social distributions of costs and health benefits, and the potential trade-offs that may exist between maximising total health and reducing health inequality. This is the first paper to show how DCEA can be applied in LMICs. Using the introduction of rotavirus vaccination in Ethiopia as an illustrative example, we analyse a hypothetical re-designed vaccination programme, which invests additional resources into vaccine delivery in rural areas, and compare this with the standard programme currently implemented in Ethiopia. We show that the re-designed programme has an incremental cost-effectiveness ratio of US$69 per health adjusted life year (HALY) compared with the standard programme. This is potentially cost-ineffective when compared with current estimates of health opportunity cost in Ethiopia. However, rural populations are typically less wealthy than urban populations and experience poorer lifetime health. Prioritising such populations can thus be seen as being equitable. We analyse the trade-off between cost-effectiveness and equity using the Atkinson inequality aversion parameter, ε, representing the decision maker's strength of concern for reducing health inequality. We find that the more equitable programme would be considered worthwhile by a decision maker whose inequality concern is greater than ε=5.66, which at current levels of health inequality in Ethiopia implies that health gains are weighted at least 3.86 times more highly in the poorest compared with the richest wealth quintile group. We explore the sensitivity of this conclusion to a range of assumptions and cost-per-HALY threshold values, to illustrate how DCEA can inform the thinking of decision makers and stakeholders about health equity trade-offs.

Introduction

Tackling inequalities is a key feature of global health policy agendas and underpins the sustainable development goals and associated universal health coverage movement (Marmot et al., 2012, United Nations, 2015, Ottersen et al., 2014). However, methods of cost-effectiveness analysis (CEA) used in mainstream healthcare decision making focus on the objective of maximising population health rather than reducing unfair health inequalities (Sassi et al., 2001, Weatherly et al., 2009, Johri and Norheim, 2012). Recent methodological advances have enhanced CEA methods to enable them to go beyond the mythical 'average' citizen and consider the social distribution of costs and benefits (Cookson et al., 2017). Notable amongst these methodological developments are "extended" cost-effectiveness analysis (ECEA), which provides breakdowns of costs and benefits by social groups (e.g. income, area of residence, sex), and "distributional" cost-effectiveness analysis (DCEA) which, in addition, provides summary measures of health inequality impact and analyses potential trade-offs between increasing total health and reducing health inequality (Verguet et al., 2015a, Asaria et al., 2015).

ECEA expands traditional CEA to examine the effects of an intervention on financial risk protection (safeguarding against financial hardship associated with paying for health services) as well as on health outcomes (Verguet et al., 2015a, Verguet et al., 2016). It breaks down the costs, health benefits and financial risk protection benefits by social groups (usually income groups). However, ECEA does not account for health opportunity costs of displaced expenditure within the health sector budget neither does it provide any guidance on how to resolve equity-efficiency trade-offs (Verguet et al., 2015b, Levin et al., 2015, Pecenka et al., 2015).

DCEA provides an explicit framework for analysing the social distribution of health benefits and opportunity costs and the equity trade-offs that may arise between improving total health and reducing health inequality (Asaria et al., 2015). It examines the distribution of outcomes similarly to ECEA but goes further by enabling transparent analysis of health opportunity

costs, summary measures of health inequality impact, and equity trade-offs, with the aim of providing decision makers with a clearer understanding of the health inequality impacts and trade-offs and the implications of alternative social value judgements about equity (Asaria et al., 2016). Social factors such as income, education, socioeconomic status can impact on the health of individuals over their lifetime and cause inequalities in lifetime health between social groups. DCEA facilitates the inclusion of impacts on overall inequality in lifetime health, rather than on inequality in health gains directly from the intervention, by accounting for the effects of an intervention on the distribution of lifetime health (Asaria et al., 2014). However, DCEA does not account for non-health benefits such as financial risk protection.

To date, DCEA has primarily been applied to research in England (Asaria et al., 2015), while ECEA has been used extensively to explore the distribution of outcomes of health policies in low- and middle-income countries (LMICs) (Verguet S and Jamison, forthcoming); though some previous research in LMIC settings has used some components of DCEA (Johansson and Norheim, 2011, Ngalesoni et al., 2016). In this paper we apply DCEA to an illustrative example of scaling up rotavirus vaccination in Ethiopia and show how the different components of DCEA can be applied in LMIC settings. In doing so we aim to demonstrate how to overcome the various challenges of applying these data intensive methods in relatively data sparse contexts and showcase some of the insights that such an analysis can provide to health policy makers in such contexts.

Methods

Publicly Funded Rotavirus Vaccination

Rotavirus is responsible for around a third of global diarrhoea-related deaths, the majority of which occur in LMICs (Liu et al., 2012, Tate et al., 2012). Before vaccination was introduced in 2013, Ethiopia had the fifth highest number of rotavirus related deaths (28,218 per year) worldwide. The vaccine has been found to be effective in many countries around the world, reducing severe rotavirus disease by more than 60% in the first year of life (Madhi et al.,

2010, Armah et al., 2010). The most recent estimate of vaccine coverage from Ethiopia DHS 2016 is 56%, however, coverage varies across groups (Central Statistical Agency (CSA) [Ethiopia] and ICF, 2016). Since its introduction, coverage has been lowest amongst the poor in Ethiopia (Central Statistcal Agency [Ethiopia], 2014). As more of the population in poorer wealth quintile groups live in rural areas, by targeting these areas it may be possible to increase coverage amongst the poor (Central Statistcal Agency [Ethiopia] and Living Standards Measurement Study (LSMS), 2017). However, there are higher delivery costs in rural areas due to a range of logistical challenges.

Comparing DCEA and ECEA

To illustrate the value of DCEA, we built on a previous ECEA conducted before the introduction of the rotavirus vaccine in Ethiopia (Verguet et al., 2013a). We began by evaluating the existing rotavirus vaccination programme from 2013 to 2016 (the "standard" vaccination programme), compared to the prior situation of no vaccination in 2012, using the same assumptions as the original ECEA model but updating the coverage assumptions to the levels actually achieved in different groups by 2016. We then evaluate a hypothetical alternative re-designed vaccination programme from 2013 to 2016 (the "pro-poor" vaccination programme) that would have made proportionally more effort to deliver vaccination in rural areas. We incorporated health opportunity costs into our analyses to compute "net" health gains by social group. We placed these health gains into the broader context of differences in lifetime health, and finally examined the trade-offs between cost-effectiveness and health equity. We focused on equity in terms of the distribution of health between population wealth quintiles; however, we note this is only one possible dimension by which equity may be considered. It is possible to conduct similar analysis by other dimensions of interest such as, gender, age, ethnicity, geography, if the relevant data is available.

Parameters

Parameters used to evaluate each vaccination programme are presented in **Table 1**. Rotavirus death rate, relative risk of rotavirus mortality and vaccine effectiveness were taken from the original ECEA study (Verguet et al., 2013a). All other parameters were updated to use more recent estimates or to represent the pro-poor hypothetical programme. Differential health risks were reflected in the fact that poorer children were more likely to contract rotavirus and more likely to die if they did. The vaccine was assumed to have equal effectiveness in all groups, instantaneous scale-up was assumed, with the primary health outcome being rotavirus diarrhoea deaths averted (Verguet et al., 2013a).

Costs were calculated as the vaccine cost plus the cost of delivering the vaccine and are presented in US dollars. These were applied to the population receiving the vaccine from an approximate annual birth cohort of 2,800,000, taking account of differential fertility rates by wealth quintile group (Central Statistical Agency [Ethiopia], 2014). The benefits of the vaccine were calculated as deaths averted in children under 5 years old, which were converted to healthy life years (HALYs) (essentially the same as quality adjusted life years (QALYs), see **Appendix 1** for some of the methodological nuances).

Consideration was given to how health opportunity costs – i.e. health forgone elsewhere in the system as a result of introducing the vaccine programme – were distributed among the population. The assumed distribution of the opportunity costs of reduced public healthcare expenditure is shown in **Table 1**. This inverted 'U' shape was based on the assumption that the poorest group had the lowest opportunity costs, as government health expenditure does not often reach them, while the richest group had similarly low opportunity costs as they were most likely to opt out of government funded healthcare preferring instead to purchase healthcare from private providers. Alternative assumptions were considered and are presented in **Appendix 3** along with their effect on results.

The cost-effectiveness threshold (CET) was used to assess whether an intervention improved total health, after allowing for other forgone investments. There are a range of

possible values that could be used to represent the CET for Ethiopia. For the base case analysis we made the assumption that the CET for Ethiopia was $50 per HALY. This CET was chosen for two reasons: first, it falls within the range recommended ($10-$255) in the analysis by Woods et al. (2016) and therefore represents a plausible empirical estimate of health opportunity cost in Ethiopia; second, it was chosen as it enabled us to clearly illustrate the trade-off between equity and efficiency in this example. It is notable, however, that the WHO recommended threshold range of 1-3 time GDP per capita is substantially higher ($619-$1,875). Consequently, we assess the impact of alternative CETs within the range $10-$1,857 in sensitivity analyses.

The Baseline Distribution of Lifetime Health

The baseline distribution of lifetime health describes how the overall burden of mortality and morbidity is distributed among different social groups within the general population. This allows consideration of the effects of an intervention on inequality in lifetime health, by comparing the distribution of lifetime health at baseline to that which would result following a new health intervention. Mortality and morbidity may vary by gender, age, ethnicity, wealth and many other factors. The factors that are used to estimate the distribution of lifetime health in a population will depend on the data available and the dimensions deemed relevant for the distributional evaluation undertaken. The baseline health distribution must be estimated for the general population, not just for those receiving the intervention. This is because policy concern for inequality encompasses inequality within the entire general population, and the opportunity costs of displaced resources will likely fall on members of the wider population including those who do not directly benefit from the intervention being evaluated (Asaria et al., 2016).

In the absence of reliable census and vital statistics data in Ethiopia (as is also the case in many other low-income countries), we used indirect estimates of mortality differences by social strata drawing on WHO data on healthy life expectancy (HALE) and Demographic and

Health Survey (DHS) data on morbidity and mortality by household asset wealth group in order to estimate the distribution of lifetime health. Population average HALE values, measured in HALYs, were taken from the WHO Life Expectancy database (World Health Organisation, 2015, Salomon et al., 2012). These average HALE values were weighted by mortality based on previously modelled life expectancy by socioeconomic group, drawing on DHS data on child mortality by household asset group (Tranvag et al., 2013). Finally, the values were weighted by morbidity based on available prevalence data by socioeconomic group (GBD, 2010, IHME, 2015). The groups were then ordered from least to most healthy and population weighted to create the baseline distribution of HALE at birth. Detailed descriptions of these calculations are provided in **Appendix 1**.

Equity Impact Analysis

Using the same modelling assumptions as Verguet et al. (2013a), costs (see **Table 1**), calculated as the vaccine cost plus the delivery cost, and health effects, calculated as deaths averted due to the vaccine, were estimated for each wealth quintile group (see **Appendix 2**). Costs were assigned based on the proportion of each quintile group living in urban/rural areas (Central Statistical Agency [Ethiopia], 2014). Opportunity costs and health benefits were calculated in terms of HALYs. Deaths averted were multiplied by the HALE values for the corresponding quintile group from the baseline health distribution to estimate total HALYs gained in each group, from which per capita HALY gain was calculated. Assuming a constant population over time, the additional HALYs gained were added to the baseline HALE to give an estimation of the HALE distribution after the introduction of the vaccination programme. Using the net benefit approach, total costs of the vaccine programme were divided by an assumed base-case CET value of $50 per HALY to convert costs into health opportunity costs (alternative thresholds were assessed in sensitivity analyses). Net health benefits (NHB) were thus calculated for each wealth quintile group (J) as:

$$NHB_J = \Delta\text{HALYs}_J - (\Delta Costs_J / CE\ threshold) \quad (1)$$

Equity Trade-off Analysis

To evaluate any trade-offs between improving total health and reducing inequality in health, we used an Atkinson social welfare function with relative inequality aversion parameter, ε, to represent the decision maker's strength of concern for reducing health inequality. This parameter describes the decision maker's willingness to make trade-offs between improving total health and reducing health inequality (Asaria et al., 2015). We focused on this single index of inequality aversion in order to keep the paper simple and concise. However, different social welfare functions can be used in DCEA to represent different kinds of inequality concern – for example, absolute health inequality – as illustrated by Asaria and colleagues (2015). The nature of the inequality concern should drive the selection of inequality indices and it may be useful to employ several such measures in sensitivity analyses. We used DCEA to compare the two alternative vaccination strategies in equity-cost-effectiveness space using the "health equity impact plane" in which the effect on health was quantified as in standard CEA, and the health inequality impact is quantified by the reduction in the Atkinson index offered by the "pro-poor" vaccination programme compared with the "standard" programme.

To use the Atkinson index one must choose a value for the inequality aversion parameter. A value for the inequality aversion parameter (ε) equal to 0 indicates there is no aversion to inequality and a Utilitarian perspective is represented. As the value of ε increases, higher priority is given to transfers lower in the distribution (the worse off). An empirical study in England has estimated an Atkinson relative health inequality aversion parameter as 10.95 (Robson et al., 2016). This was used as a tentative reference point for the analysis. Extensive sensitivity analysis was conducted to explore the impact of using alternative values of the inequality aversion parameter.

The equity-efficiency trade-off can be depicted by calculating the equally distributed equivalent (EDE) level of health that, if obtained by every individual, would enable a society to reach the same level of overall health as the current modelled distribution of health (Asaria et al., 2015). This allows alternative interventions or strategies to be compared for any given level of inequality aversion. The difference between a population's mean level of health and the EDE for health indicates the average amount of health per person that society (or the decision maker) is willing to sacrifice to achieve an equal distribution of health for a given level of inequality aversion, conditional on the current inequality in the population health distribution (Asaria et al., 2015). We therefore plotted EDE for each strategy at a range of levels of inequality aversion, ε, to show which option would be preferred taking account of the trade-off between overall health and health equity. We conducted equity trade-off analysis for the base case at a CET value of $50. In addition a range of alternative CET values were also used to explore the equity-efficiency trade-off in sensitivity analyses.

Results

The Baseline Distribution of Lifetime Health

Figure 1 shows the estimated baseline distribution of HALE at birth in each wealth quintile group of the Ethiopian population compared with the life expectancy in each group. The HALE values are lower than the life expectancy values because of the adjustment for morbidity. This adjustment is greater in the lower wealth quintile groups due to higher levels of morbidity in these groups.

Equity Impact Analysis

Step by step calculation of the distribution of NHB resulting from the equity impact analysis is given in Table 2 and the resulting distribution is shown in Figure 2, for each vaccination

programme compared to no vaccination. This shows that, compared with the standard programme, the pro-poor programme provides greater gains to the lowest wealth quintile groups at the expense of the higher wealth quintile groups.

Equity Trade-off Analysis

The cost-effectiveness plane, Panel A of Figure 3, shows the pro-poor vaccine compared to the standard vaccine as would be presented in standard CEA. The pro-poor vaccine is not cost-effective at a threshold of $50 per HALY as compared to the standard vaccination programme. However, using the "health equity impact plane" shown in Panel B of Figure 3 we compare the two strategies in equity-cost-effectiveness space. The pro-poor vaccine falls in the south-east "lose-win" quadrant (CET=$50), demonstrating that relative to the standard vaccination programme it has a positive impact on health equity despite its negative impact on total health. Thus, a trade-off occurs between improving total health and reducing socioeconomic inequality in health. Figure 3 also presents the equity trade-off analysis at the four CET values selected for the sensitivity analyses to show how the choice of threshold impacts on the results.

The difference in the EDE health of the two vaccination strategies at a range of levels of relative inequality aversion, ε, are depicted in Figure 4. If inequality aversion is zero then the EDE is equal to the mean health and, at a CET of $50, the standard programme would provide 7,395 more population HALYs than the pro-poor programme. For inequality aversion parameters greater than ε=5.66, the point at which the line crosses the x-axis, the pro-poor programme is preferred, implying that the decision maker is willing to sacrifice the additional 7,395 HALYs in pursuit of lower health inequality. At this level of inequality aversion this would require that health gains in the poorest wealth quintile group were weighted at least 3.86 times more highly than health gains in the richest. No research exists on the level of inequality aversion in Ethiopia. The appropriate level of this parameter is a matter for decision makers in Ethiopia, and we acknowledge both that English views are not directly

relevant to Ethiopia and that there is uncertainty and potential for bias in the findings for England. However, if there is similar inequality aversion in Ethiopia as has been estimated in England, the concern for inequality is large enough to choose the pro-poor vaccination programme at the CET of $50.

The equity trade-off analysis at the four CET values selected for the sensitivity analyses are also depicted in Figure 4. At a CET of $10, the line lies above the x-axis and never crosses it meaning that no matter how great the inequality aversion is, the pro-poor programme would never be preferred because at this threshold the net health benefits are large enough that they are valued more highly than the gains in equity. For CETs of $255, $619 or $1,857, the opposite is true. These lines lie below the x-axis and never cross it meaning that no matter how small the inequality aversion the pro-poor programme will always be preferred because at these thresholds the net health benefits are small enough in relation to the equity benefits that the gains in equity are valued more highly than the net health benefits. For the comparison between the standard- and the pro-poor- vaccine programme, a trade-off between equity and efficiency exists for thresholds between $27.95 and $69.45.

Discussion

In this work, we illustrated the use of DCEA in LMIC settings, using the example of alternative designs of the rotavirus vaccination programme in Ethiopia and focusing on the added value and insights that may be obtained from the methods of DCEA and ECEA in designing and evaluating such programmes.

The results of the DCEA study confirmed those of the previously conducted ECEA study (Verguet et al., 2013a), that the standard vaccination programme introduced in Ethiopia was cost-effective as compared with the prior situation of no vaccination coverage, The analysis also confirmed that the vaccination programme delivered greater health benefits to poorer groups despite introducing inequality in coverage levels favouring wealthier social groups and urban areas. We built on this analysis to examine an alternative design to the

vaccination programme to address the social inequality in coverage. DCEA analysis of this re-designed programme found that such a programme would not be cost-effective relative to the standard programme but would reduce both inequality in coverage, and in health. By analysing the trade-off between cost-effectiveness and equity we found that the more equitable, pro-poor, programme would be preferred by a policy maker whose degree of inequality concern was greater than ε =5.66. At current levels of health inequality in Ethiopia, this implied that additional health gains in the poorest wealth quintile group would need to be weighted approximately 4 times as highly as health gains in the richest for the re-designed programme to be preferred. Unlike ECEA, the DCEA methodology focused solely on health impacts and did not capture financial risk protection benefits or other non-health benefits related to household wellbeing.

Our study has a number of limitations. We made simplifying assumptions around issues such as: cost savings from future treatment costs, morbidity benefits, herd effects and transmission effects. These all will result in the gains form the vaccine being underestimated. However age at death was not incorporated into the analysis, instead, overall healthy life expectancy was used to account for death averted which will result in the gains from the vaccine being overestimated.

The lack of a vital registration system for adult mortality in Ethiopia meant that we had to instead rely on the use of child health data for modelling the health. Whilst rotavirus diarrhoea mainly affects children under five years old, the lack of adult data may be a more significant limitation for evaluations of interventions for diseases that affect older age groups. Additionally, to account for morbidity in the baseline health distribution, we used prevalence data for only three diseases, though these were chosen based on their contribution to the burden of disease in Ethiopia (GBD, 2010, IHME, 2015).

Another issue requiring value judgement is the choice of health outcome metric and how far this may indirectly discriminate against disadvantaged groups. There is a large ethics and economics literature on how the health-adjusted life year (HALY) and other outcome metrics

commonly used in health economic evaluation may implicitly discriminate against preventing mortality among relatively unhealthy population groups such as the poor, the elderly and the disabled (Edlin et al., 2013). This indirect discrimination occurs because relatively few years of healthy life are gained from averting the death of a relatively unhealthy individual. It is important for producers and users of health economic evaluation to consider this ethical issue, and how far it may or may not be relevant to the case in hand. Where the issue is considered relevant by stakeholders, analysts can address it using sensitivity analysis based on simple binary outcome metrics – such as mortality or cases of disease averted – which do not indirectly discriminate in this way although they provide an incomplete and potentially misleading picture of the overall health gains in other ways, as documented in the standard health economic evaluation literature (Drummond et al., 2015).

The main strengths of DCEA are that it provides a summary measure of health inequality impact and allows explicit analysis of the trade-offs that can occur between maximising total health and reducing unfair inequality in health. There may be cases where such trade-offs do not occur, for example, if policies fall in the “win-win” quadrant of the equity-impact plane, improving both total health and reducing health inequality. However, it will often be the case that by paying closer attention to additional delivery costs to reach the most disadvantaged groups and accounting for these implementation costs at the analysis stage will lead to more equitable policies being pursued.

DCEA serves a valuable purpose, particularly for LMIC contexts, as it facilitates the consideration of fairer options so that the consequences of alternative uses of very scarce resources can be explicitly quantified in terms of both equity and cost-effectiveness. Through the analysis of trade-offs, DCEA can help with the assessment of policy alternatives so that informed decisions can be made when considering policy implementation. Additionally, use of equity parameters can help with the development of equity ‘benchmarks’ for policy makers to compare across different decisions and policy choices. This can be particularly useful as a

way to understand the impact of policy decisions and facilitates transparency and consistency of decision making.

A number of future research directions would be of value in this area. More research on the distribution of opportunity costs and also on levels of health inequality aversion would be of value. This is true for both high-income countries and LMICs. While there has been research in this area conducted for England (Robson et al., 2016), research of this kind repeated in other settings would inform further research and analyses using DCEA in other global contexts,. Finally, as has been noted elsewhere (Grimm et al., 2010), data availability is often a fundamental limitation to such analyses both in terms of vital statistics collection but also in terms of variation in vital statistics and delivery costs by equity-relevant parameters.

Conclusion

Policy makers in LMICs face difficult choices about which services to cover and how to scale up on the path to universal health coverage. This paper has outlined how DCEA can be used to extend current methods of economic evaluation of healthcare in LMICs so that trade-offs between improving total health and reducing health inequalities can be quantified and analysed in order to inform the decision making process.

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Appendices

Appendix 1

Computation of distribution of health for Ethiopia

This section describes the methods used to compute the distribution of healthy life expectancy in Ethiopia. In the absence of reliable data that can provide population estimates of mortality by social strata, we draw on WHO data on healthy life expectancy (HALE) and Ethiopia Demographic and Health Survey (EDHS) data on morbidity and mortality by household asset group. The computation involves three stages which are explained below and in **Appendix Table 1.**

Stage 1: Healthy Life Expectancy

Healthy life expectancy (HALE) is a summary measure of population health and is measured in healthy life years (HALYs). It is developed using Sullivan's method applied to country life tables and age-sex-specific estimates of severity-adjusted equivalent years of healthy life lost as a fraction of total years lived by each age-sex group. The latter is calculated by summing years of healthy life lost due to disability (YLD) across a comprehensive set of disease and injury causes drawing on analyses from the Global Burden of Disease study (WHO, 2014). HALE is now included in WHO life expectancy datasets and they define HALE as the "average number of years that a person can expect to live in "full health" by taking into account years lived in less than full health due to disease and/or injury" (WHO, 2016). HALE was chosen as the starting point for the analysis as it uses more detailed data on morbidity than rival approaches such as disability-free life expectancy, which only use binary morbidity data on whether or not a person has disability. By contrast, HALE uses cardinal data on health-related quality of life based on disease prevalence and public views about health loss associated with different disease states (Salomon et al., 2012). Through the inclusion in WHO datasets, HALE is also available for a wide range of countries, which is of particular

importance when data limitations are so prominent. HALE values give average measures of population health that take account of both quality and length of life, and therefore provide a reasonable starting point.

Stage 2: Adjust HALE according to distribution of mortality

The second stage involves weighting the average HALE values to reflect the distribution of mortality among the population. We use wealth quintile groups to reflect the different groups in the population. As no life expectancy data that is disaggregated by social characteristics is available, modelled life expectancies by wealth quintile (taken from Tranvag et al., 2013) were used to calculate relative weights which were applied to the average HALE values for males (54 HALYs) and females (56 HALYs) (WHO, 2015). The modelled life expectancy values were calculated using a modified logit life table system which requires stratified under-5 and adult mortality data. Under-five mortality data by gender, urban-rural residence and wealth quintiles from the 2011 EDHS was used. In 2011 the EDHS surveyed 17,817 households 31% in urban areas and 69% in rural areas, interviewing 16,515 women and 14,110 men. Adult mortality rates by the same groups were not available and were, therefore, calculated using adult mortality and life expectancy from the Global Burden of Disease study 2010 and weighted ratios of under-5 mortality rates for the respective groups (see Tranvag et al., 2013 for full explanation). The relative weights were calculated by assuming the modelled life expectancy of the middle wealth quintile, Q3, was equal to the mean life expectancy, and relative weights for the other quintile groups were calculated accordingly. By assuming that the distribution of life expectancy applies equally to the morbidity and mortality components of the HALE, these weights were applied as relative adjustment factors to the average HALE values to produce a distribution of HALE that reflects the distribution of life expectancy among the population according to their wealth.

Stage 3: Adjust HALE according to distribution of morbidity

The third stage involves weighting the HALE values obtained in Stage 2 to reflect the distribution of mortality among the population using the same wealth quintile groups. This adjustment was based on data on the prevalence of disease disaggregated by wealth quintile group taken from the Ethiopia Demographic and Health Survey (Central Statistical Agency and ICF International, 2012). Of the available diseases for which prevalence data was available, those selected to form the basis of the adjustment were anaemia, diarrhoea and acute respiratory infection (ARI) in children. This selection was based on the diseases that accounted for the largest burden of disease according to the Global Burden of Disease study and was restricted to three diseases because of the limited number of diseases and health issues for which data is available (GBD, 2010, IHME, 2015). Only the prevalence in children was used because of the limited data on adult morbidity that was available. Consequently, for the morbidity adjustment it was assumed that there is equal morbidity in adults as in children. The average morbidity prevalence was calculated from the 3 diseases selected and was then subtracted from 100 to equate to the prevalence of good health. This was then used to calculate the relative adjustment factors for quality of life in the same way as for the adjustment for the distribution of life expectancy – assuming that the prevalence of good health for Q3 was equal to the average. By applying these relative adjustment factors to the HALE values obtained in Stage 2, a HALE distribution reflecting both the distribution of morbidity and the distribution of life expectancy was obtained. As before, this assumed that the morbidity adjustment applies equally to the morbidity and mortality components of HALE.

The baseline health distribution

Following the adjustments for quality and length of life outlined above, the groups were ordered from least to most healthy and adjusted for the size of the group to produce a population distribution of HALE at birth (see **Figure 1** of main text).

Assumptions

Like many methods used in practice in the global health field, our approach involves making a number of assumptions in order to extract useful information from imperfect data. The assumptions made for this computation are as follows:

1. The distribution of life expectancy applies equally to the morbidity and mortality components of the HALE.
2. The distribution of morbidity applies equally to the mortality and morbidity components of the HALE.
3. For the relative weighting used, it was assumed that wealth quintile 3 was equal to the average.
4. The use of some child mortality data when modelling the distribution of life expectancy assumes that if child mortality is weighted properly, it is a valid proxy for adult mortality
5. The use of child prevalence data to create morbidity weights assumes that there is equal morbidity in adults.

As more reliable data becomes available the assumptions used to compute distributions of health in the future will become much less limiting.

Appendix 2

Calculation of costs and health effects of the vaccine programme

Costs and health effects of the vaccination programme were estimated using the same models as Verguet et al. (2013a). Rotavirus deaths averted ($DRV_{Post,J}$) were modelled as follows:

$$DRV_{Post,J} = \frac{1}{5} V_{eff}(Cov)(RR_J)(DRV_{Total})$$

Where, V_{eff} is rotavirus vaccine effectiveness, Cov is coverage achieved by the vaccine programme, RR_J is the relative risk of under-five mortality in wealth quintile J and DRV_{Total} is the total number of under-five deaths due to rotavirus before the programme (Verguet et al., 2013b).

Costs incurred per capita (TC_{RV}), from a government perspective, of implementing the programme were also calculated as:

$$TC_{RV} = 2Cov(C_{vaccine} + C_{programme})$$

Where, $C_{vaccine}$ is the cost per dose of the vaccine and $C_{programme}$ is the cost per dose of the programme (Verguet et al., 2013b).

All parameters used within the above model calculations are reported in Table 1 of the main paper.

Appendix 3

Distribution of opportunity cost

In the primary analysis the opportunity costs – i.e. the health that is given up elsewhere in the system as a consequence of the additional costs incurred by introducing the vaccine programme – are assumed to take an inverted 'U' shaped distribution. This is based on the assumption that the poorest group will have the lowest opportunity costs, as coverage often does not reach them, while the richest group will have similarly low opportunity costs as they are most likely to take advantage of private healthcare. An assumption around the distribution of opportunity costs was necessary given the lack of data. However, alternative assumptions around the distribution of opportunity costs were also explored. They are presented here, along with the effect the different assumptions have on the results.

The alternative assumptions around the distribution of opportunity costs that were explored are as follows:

1. Opportunity costs borne proportionately more by high income groups
2. Opportunity costs borne proportionately more by low income groups
3. Opportunity costs equally distributed across all wealth quintile groups

For each case, the proportion of opportunity cost borne by each wealth quintile group is presented in **Appendix Table 2.** The resulting distributions of net health effect in each case are presented in **Appendix Figures 1-3**. This shows how the assumption taken on the distribution of opportunity costs can impact the results and the conclusions drawn highlighting the importance of careful consideration of the distribution of opportunity costs within an analysis and also the need for further research in this area.

Table 1: Base case parameters used to model each scenario

Parameters that are the same across vaccination programmes				**Source**
Population (annual cohort of live births)	2,800,000			Based on (Central Statistical Agency [Ethiopia], 2014)
Urban	467,622			
Rural	2,332,378			
Rotavirus death rate per 1000 live births	5.4			Based on (Liu et al., 2012, Tate et al., 2012)
Relative risk ratio of rotavirus mortality				Based on (Rheingans et al., 2012)
Ratio of poorest to richest quintile group	2.9			
Risk index, poorest to richest quintile group	1.34, 1.23, 1.06, 0.91, 0.46			
Vaccine effectiveness (%) (per 2-dose course)	49			(Madhi et al., 2010)
Vaccine price (per 2-dose course)	$5.00			(Global Alliance for Vaccines and Immunization)
Vaccine price with GAVI subsidy (per 2-dose course)	$0.40			
Cost-effectiveness threshold (base case)	$50			Based on (Woods et al., 2016)
Cost-effectiveness threshold range (sensitivity analyses)	$10-$1,857			Based on (Woods et al., 2016, Evans et al., 2005)
Distribution of opportunity cost (proportion of cost borne by the poorest to richest quintile group)	0.185, 0.21, 0.21, 0.21, 0.185			Assumed
Parameters that differ across vaccination programmes				
	No Vaccination	**Standard Vaccination[1]**	**Pro-poor Vaccination[2]**	**Source**
Incremental vaccination delivery cost (per 2-dose course)				Based on (Atherly et al., 2012, Wolfson, 2008, Le Gargasson et al., 2015, Schütte et al., 2015)
Urban	$0	$0.50	$0.50	
Rural	$0	$0.50	$1.00	
Vaccination coverage (%) (average proportion receiving the 2-dose course)	0	56	62	[1](Central Statistical Agency (CSA) [Ethiopia] and ICF, 2016); [2]Hypothetical
Within group vaccination coverage (%) (poorest to richest quintile group)	0	46, 49, 52, 63, 78	56, 56, 56, 63, 78	[1](Central Statistical Agency (CSA) [Ethiopia] and ICF, 2016); [2]Hypothetical
Parameter uncertainty ranges are not included as this is an illustrative example.				

Table 2: Equity Impact Analysis

Wealth Quintile Group	Population births[1]	Population after rotavirus deaths (no vaccination)	Cost to vaccinate group[2] (US$)			Deaths Averted		
			Standard	Pro-poor	Difference[4]	Standard	Pro-poor	Difference[4]
Q1 (poorest)	677,419	673,367	1,881,870	2,191,311	309,441	919	1112	193
Q2	643,548	639,829	1,899,755	2,210,809	311,054	897	1021	124
Q3	598,387	595,182	1,863,377	2,159,122	295,745	815	880	65
Q4	564,516	561,764	2,137,258	2,451,673	314,415	851	851	0
Q5 (richest)	316,129	314,738	1,481,381	1,570,513	89,132	532	532	0
Total	**2,800,000**	**2,784,880**	**9,263,642**	**10,583,428**	**1,319,786**	**4,014**	**4,395**	**381**

Wealth Quintile Group	Population HALYs Gained			Health opportunity costs (HALYs)[3]			Net health effect (HALYs)		
	Standard	Pro-poor	Difference[4]	Standard	Pro-poor	Difference[4]	Standard	Pro-poor	Difference[4]
Q1 (poorest)	43,642	52,786	9,144	34,275	39,159	4,884	9,367	13,627	4,260
Q2	45,647	51,956	6,309	38,907	44,450	5,543	6,740	7,506	766
Q3	44,920	48,469	3,549	38,907	44,450	5,543	6,013	4,019	-1,994
Q4	46,115	46,115	0	38,907	44,450	5,543	7,207	1,664	-5,543
Q5 (richest)	32,065	32,065	0	34,275	39,159	4,884	-2,211	-7,094	-4,883
Total	**212,389**	**231,390**	**19,001**	**185,273**	**211,669**	**26,396**	**27,116**	**19,722**	**-7,394**

[1]Based on fertility rate by quintile (DHS Ethiopia 2011)

[2]Based on within group coverage, proportion in urban/rural areas and associated cost

[3]Total opportunity cost is calculated as the total cost (from column 3 of the top half of the table) and a cost per HALY of $50 (Woods et al., 2016). Opportunity costs for each group are calculated as the total opportunity cost multiplied by the fraction of opportunity cost that falls to each quintile, assuming an inverted 'U' shaped distribution of opportunity cost (the distribution of opportunity cost is reported in Table 1)

[4]Difference=pro-poor-standard

Note: The rich gain the least even with lower opportunity cost because they are the least at risk.

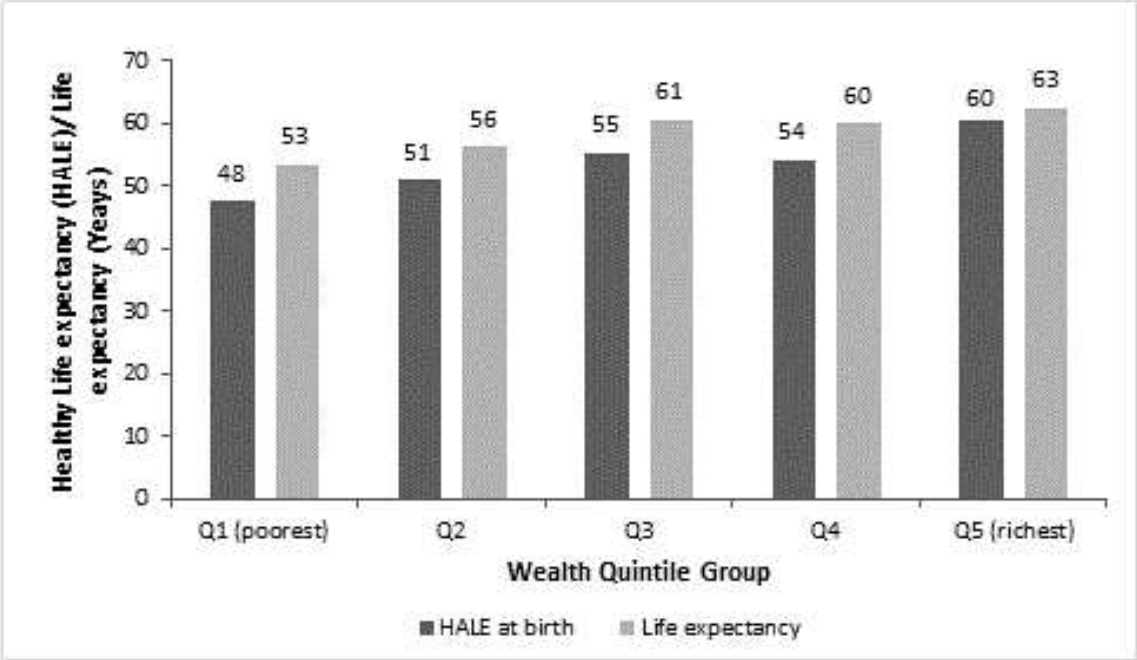


Figure 1: Population distribution of health in Ethiopia: HALE at birth compared to Life expectancy (life expectancy from Tranvag et al., 2013)

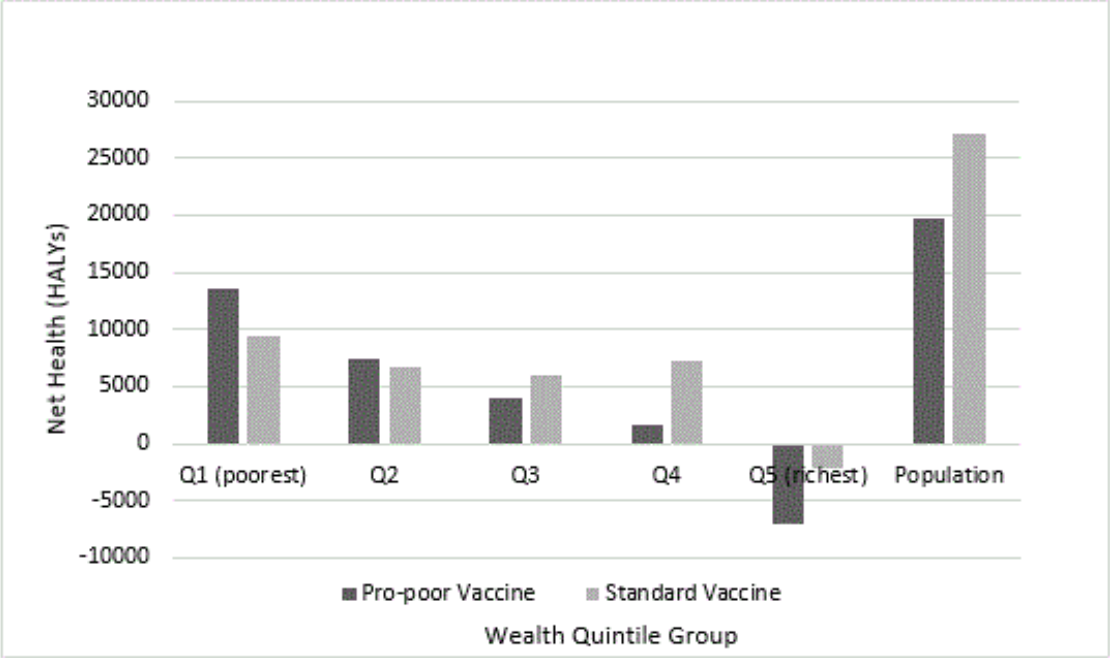


Figure 2: Net health effect of each programme compared to no vaccination (λ=$50)

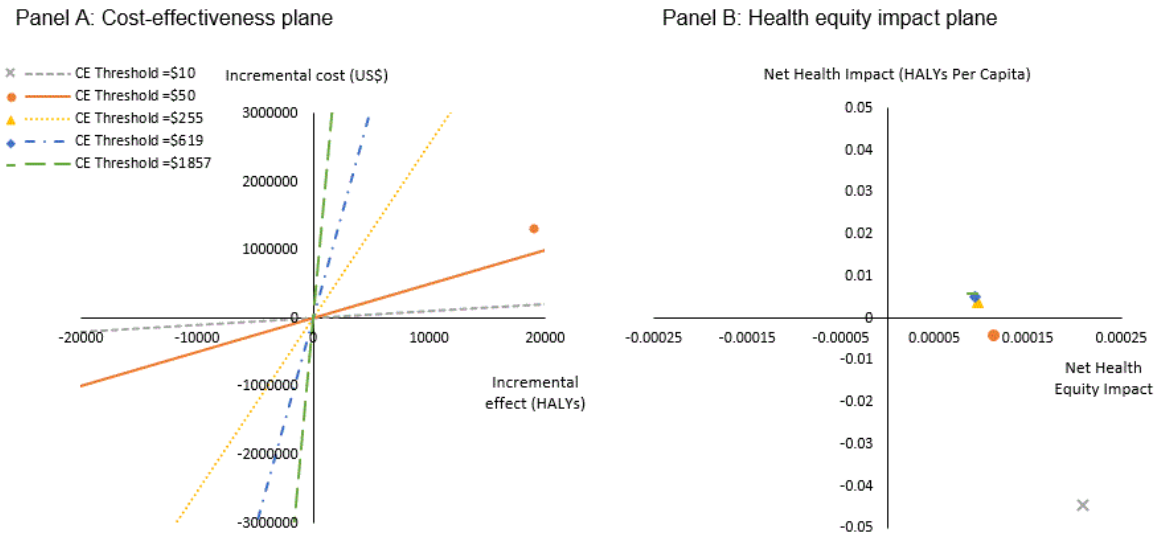


Figure 3: Incremental analysis of pro-poor vaccine compared to standard vaccine: Cost-effectiveness plane vs. Health equity impact plane

Note: Panel A plots the gross health effect; Panel B plots the net health effect (taking account of opportunity cost). The Atkinson index of inequality is normally scaled from 0 to 1, where 1 represents full inequality, but we have reversed the scale so that a positive impact represents improved equity.

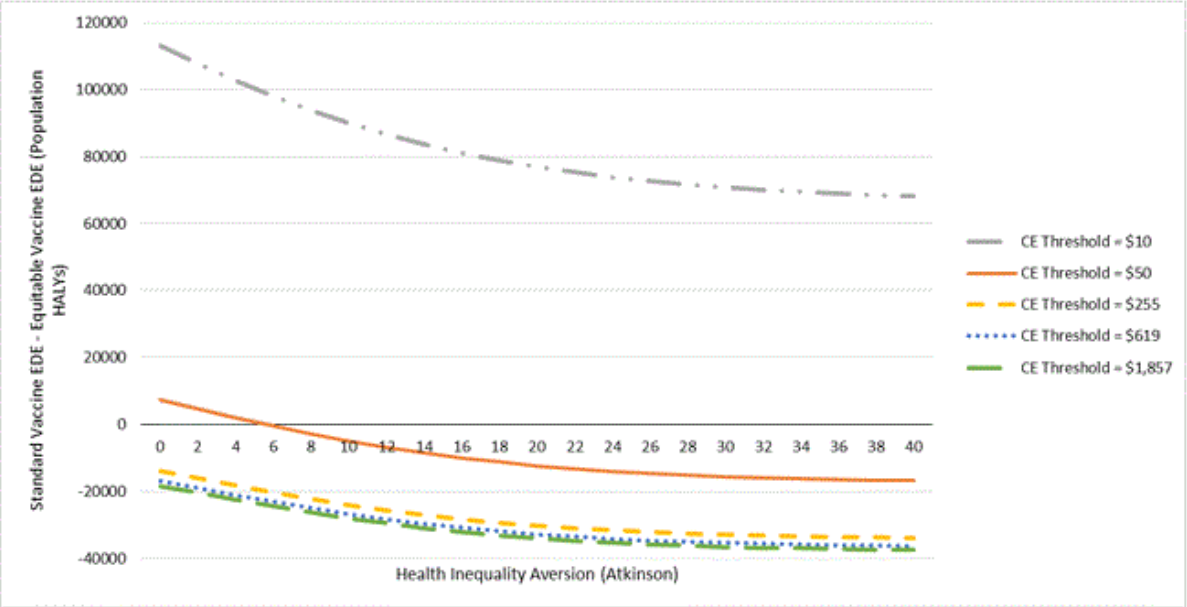


Figure 4: Equity trade-off analysis

Notes: 1) The health inequality aversion (x-axis) represents the strength of concern for reducing health rather than improving total health. 2) At the point the line crosses the x axis: to the left it is better to implement the standard programme, to the right it is better to implement the pro-poor programme.

Appendix Table 1: Modelling the baseline health distribution

Stage 1			Stage 2				Stage 3			
*Average HALE		Wealth Quintile	*Modelled Life expectancy	Adjustment Factor (LE)	Adjusted HALE		100- Average Morbidity Prevalence	Adjustment Factor (QoL)	Adjusted HALE	
Female	Male				Female	Male			Female	Male
		Q1	53.4	0.88	49.35	47.58	76.5	0.97	48.19	46.47
		Q2	56.2	0.93	51.93	50.08	78	0.99	51.71	49.87
56	54	Q3	60.6	1	56	54	78.33	1	56	54
		Q4	59.9	0.99	55.35	53.38	77.97	0.99	55.09	53.13
		Q5	62.5	1.03	57.76	55.69	82.97	1.06	61.17	58.99

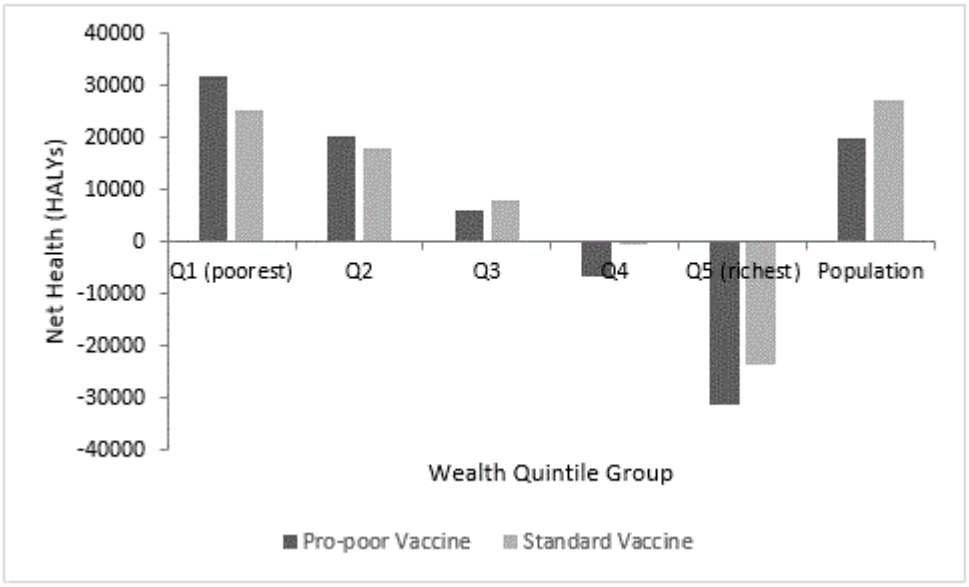
***Source: WHO, 2015**

****Source: Tranvag, Ali & Norheim, 2013**

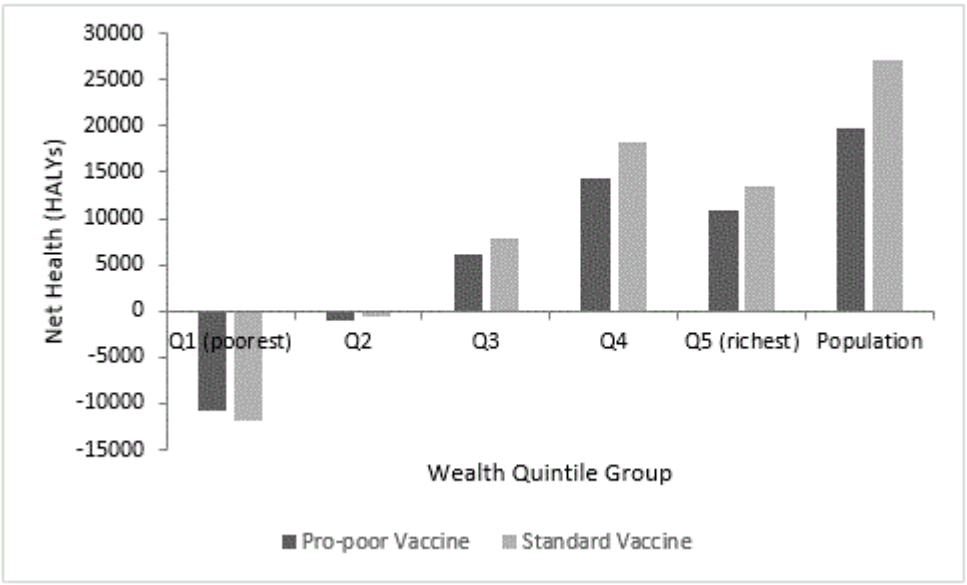
Appendix Table 2: Proportion of opportunity cost assigned to each wealth quintile group

Wealth Quintile Group	Vaccination			
	Base case	More high income	More low income	Equal
Q1	0.185	0.1	0.3	0.2
Q2	0.21	0.15	0.25	0.2
Q3	0.21	0.2	0.2	0.2
Q4	0.21	0.25	0.15	0.2
Q5	0.185	0.3	0.1	0.2

Appendix Figure 1: Net health effect of vaccination compared to no vaccination (λ=$50) – Opportunity costs borne more by high income



Appendix Figure 2: Net health effect of vaccination compared to no vaccination (λ=$50) – Opportunity costs borne more by low income



Appendix Figure 3: Net health effect of vaccination compared to no vaccination (λ=$50) – Opportunity costs equally distributed