Falling Short of Expectations: Improving Policy Design in Global Health

FALLING SHORT OF EXPECTATIONS: IMPROVING POLICY DESIGN IN GLOBAL HEALTH

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Abstract

This dissertation is comprised of three studies that examine three global and national-level policies, and apply different quantitative analyses to improve the research base that informs these policies, with the aim of ultimately improving the designs of existing health policies. Chapter 2 examines the UNAIDS' goal to eliminate AIDS by 2030. It combines survival analysis of a longitudinal dataset and a Markov model of progression through different stages of HIV care cascade, and find that the mathematical models that informed the UNAIDS' policy overestimates the health benefits that could be realized in real life. Chapter 3 examines South Africa's Integrated Chronic Disease Management model, using regression models I conclude that how different types of multimorbidity affects the care patients receive should be considered when designing care delivery in order to provide coherent and efficient care. Chapter 4 assesses the target set by the Global Vaccine Action Plan, which aims to improve health equity through providing equal access to vaccines. I developed a methodology to quantify the impact of different vaccine coverage scenarios with respect to household income that take into account the distribution of other risk factors. I conclude in this chapter that merely ensuring equal access to vaccines will not reduce health outcome gaps across income quintiles because of the differences in the distribution of risks and the treatment provided.

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I joined the Department in the Fall of 2012 with limited research experience in global health. Despite my lack of experience, my committee members patiently guided me through my first years and trained me to become an independent researcher. Michael Reich, my advisor, guided me through big and small decisions, and continuously asked tough questions and challenged me to think critically. In my first year, I quickly identified Josh Salomon as someone I would like to work with, and with his mentorship, I learned to identify good research questions and apply rigorous thinking. All three of my dissertation chapters benefited greatly from his support. Stephen Resch was my go-to person for brainstorming sessions. Every few weeks I brought a list of potential research ideas to his office, and now in hindsight, most of them were not great, but Stephen was always encouraging and patient in helping me develop the ideas. In fact, my first first-author paper came out of these brainstorming sessions. Writing this dissertation would not have been possible without the support of this wonderful committee.

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I would like to dedicate this dissertation to the individuals we in global health aim to serve. I sincerely believe that good research can lead to better health policies, and thus improve population health. My belief that our work may contribute even a little bit to improving their wellbeing is what motivates me every day.

Chapter 1. Introduction

During my doctoral studies, I have learned to appreciate the important role research plays in informing global health policies. I have had the opportunity to be involved in dialogues between policymakers and researchers, and realized that what we as researchers do have the potential to impact health policies, and ultimately, improve population health. However, I also observed that the flaws of existing health policies can often be attributed to the poor quality of the research that informed the design. The poor quality could be explained by several reasons, such as unavailability of data, poor study design, lack of attention to details, and not enough time to conduct appropriate studies.

In this thesis, I examine three global and national-level policies, and apply different quantitative analyses to improve the research base that informs these policies, with the aim of ultimately improving the designs of existing health policies. Chapter 2 examines the UNAIDS' goal to eliminate AIDS by 2030, and I argue that the mathematical models that informed this policy overestimates the health benefits that could be realized in real life. Chapter 3 examines South Africa's Integrated Chronic Disease Management model, and I conclude that how different types of multimorbidity affects the care patients receive should be considered when designing care delivery in order to provide coherent and efficient care. Chapter 4 assesses the target set by the Global Vaccine Action Plan, which aims to improve health equity through providing equal access to vaccines. I conclude in this chapter that merely ensuring equal access to vaccines will not reduce health outcome gaps across income quintiles because of the differences in the distribution of risks and the treatment provided.

Chapter 2, titled "Improving the validity of mathematical policy models for HIV elimination by incorporating empirical estimates of progression through the HIV treatment cascade", examines the common assumptions built into published HIV mathematical model results and compares their estimated health benefits to results from a model that reflects real-life HIV cascade of care. With co-authors Joshua Salomon, Noah Haber, Till Bärnighausen, Kobus Herbst, and Dickman Gareta, I conclude that the evidence base for increasing treatment threshold for HIV is overestimating the benefits by a significant amount, and in

order to move towards more realistic and policy-relevant studies, a more complete set of the constraints in the cascade into mathematical models are needed.

Chapter 3, titled "The effect of concordant and discordant diseases on effective coverage for hypertension, diabetes, and HIV among older adults with multimorbidity", takes a multimorbidity perspective to improve the implementation of South Africa's Integrated Chronic Disease Management (ICDM) model. With co-authors Joshua Salomon, F. Xavier Gómez-Olivé, Jennifer Manne-Goehler, Alisha Wade, and Stephen Tollman, I assessed the relationship between different types of multimorbidity (concordance/discordance, defined as those with similar/different pathophysiologic risk profile with similar/different management plans) and one's progression along the care continuum for hypertension, diabetes, and HIV care. The findings suggest that the objective of the ICDM to coordinate and enhance the management of co-existing diseases has not yet been met partially because the interactions between multimorbidity and care seeking were not understood and incorporated in the design of the policy. In populations with high prevalence of multimorbidity, the effect of different types of multimorbidity on the progression along the care cascade should be studied and incorporated into the design of the healthcare delivery system.

Chapter 4, titled "Estimating the distribution of morbidity and mortality of childhood diarrhea, measles, and pneumonia by socio-economic group in low- and middle-income countries", questions one of the key objectives of the Global Vaccine Action Plan (GVAP), which aims to improve health equity through providing equal access to vaccines. With coauthors Stéphane Verguet, Carlos Rimuallo-Herl, Joshua Salomon, Stephen Resch, and Logan Brenzel, I developed a methodology to quantify the impact of different vaccine coverage scenarios with respect to household income that take into account the distribution of other risk factors. I find that, in contrast to what GVAP suggests, merely ensuring ensuring equal access to vaccines will not lead to health equity. In fact, depending on how one defines equity, providing equal access to vaccines may in fact increase inequity.

To summarize, this thesis reviewed some of the underlying assumptions and evidence base of existing global health policies. These papers are currently ongoing journal submission processes, and I hope they would generate conversations with policymakers and international agencies that introduced these policies to improve the design and ultimately have a larger impact on population health.

Chapter 2. Improving the validity of mathematical policy models for HIV elimination by incorporating empirical estimates of progression through the HIV treatment cascade

Angela Y. Chang, Noah Haber, Till Bärnighausen, Kobus Herbst, Dickman Gareta, Joshua A. Salomon

2.1 Abstract

Background

Current optimism regarding prospects for eliminating HIV by expanding antiretroviral treatment has been emboldened in part by projections from several mathematical modeling studies. Drawing from a detailed empirical assessment of rates of progression through the HIV care cascade, this chapter aims to quantify the extent to which models may overestimate health benefits from policy changes when they fail to incorporate a realistic understanding of the cascade.

Methods

We estimated rates of progression through stages of the HIV treatment cascade using data from a longitudinal population-based HIV surveillance system in rural KwaZulu-Natal, South Africa. Incorporating empirical estimates in a mathematical model of HIV progression, infection transmission, and care, we estimated mortality and secondary infections averted under a range of treatment scale-up scenarios, reflecting expanding treatment eligibility thresholds from CD4 200 to 350, 350 to 500, and 500 cells/mm^3 to treating all HIV-positives irrespective of their CD4 count, and compared the results to those implied by the optimistic assumptions that have been commonly adopted by existing models.

Results

Health benefits, namely years of life gained and HIV transmission averted, from expanding the treatment eligibility threshold from CD4 200 to 350 and 350 to 500 cells/mm^3 may be overestimated by two to five-fold in models that fail to capture realities of the care cascade. In the case of raising the HIV treatment eligibility threshold from CD4 500 cells/mm^3 to treating everyone irrespective of their CD4 count, which is the current WHO recommendation, health benefits gained from this policy change may be overestimated by approximately 15 to 21-fold.

Conclusions

Health benefits projected from existing HIV models using optimistic assumptions may be largely overestimated. As implementation of treatment scale-up proceeds, it is important to assess the effects of required scale-up efforts in a way that incorporates empirical realities of how people move through the HIV cascade.

2.2 Keywords

HIV, treatment eligibility, cascade of care, mathematical modeling, antiretroviral treatment

2.3 Introduction

Ambitious global targets have been established to bring an end to the HIV/AIDS epidemic. The Sustainable Development Goals and the United Nations General Assembly endorsed the goal to end the AIDS epidemic by 2030 (1,2). The Joint United Nations Programme on HIV/AIDS (UNAIDS) urged countries to adopt a "Fast-Track" approach defined by targets known as 90-90-90: 90 percent of people living with HIV knowing their HIV status, 90 percent of those with known status being on antiretroviral treatment (ART), and 90 percent of those on treatment with suppressed viral loads, as means to ending the epidemic by 2030 (3).

Optimistic prospects for the elimination of HIV are in part based on recent positive research findings regarding the efficacy of treatment as prevention (TasP) (4) and immediate initiation of ART upon diagnosis, known as the 'test-and-treat' model (5). Several mathematical models were constructed to estimate the potential health impacts of TasP. However, models often assume high rates of uptake (6–8), coverage (6,9), and adherence (5,6,10), without specifying how they will be achieved nor include costs that reflect these additional activities and interventions. In contrast to the favorable assumptions in many modeling studies, empirical studies have produced mixed results for TasP (11–14), reporting relatively poor or inconsistent results for linkage to care (11) and retention (12). For example, the ANRS 12249 study in rural South Africa (14) found minimal effects of TasP in increasing the proportion of HIV-positive patients linking to care and achieving viral suppression when compared to standard of care. Contrary to the common belief that TasP avoids operational difficulties in linking patients to care for assessing eligibility and instead directly initiating them on ART (5), this trial found no significant difference in the proportion linked to care within 6 and 12 months between the TasP and control arms (14), possibly because these individuals were asymptomatic and thus did not recognize immediate benefits of linkage to care or treatment initiation. In contrast, the SEARCH study, a community-based multi-disease approach to HIV test-and-treat model in rural Kenya and Uganda, achieved a significant improvement in linking HIV-positive patients to care but only through resource-intensive large community health campaigns and frequent adherence interventions (13).

Mathematical models often are instrumental in informing policies and strategic directions towards ambitious elimination targets. As implementation of treatment scale-up proceeds, it is important to assess costs and effects of required scale-up efforts in a way that incorporates empirical realities of how people move through the HIV care cascade (15). This is crucial both in terms of setting realistic expectations and making feasible plans for what can be achieved at a certain cost, and for focusing on specific aspects of the cascade that require a suite of interventions that collectively comprise a scale-up strategy. Drawing from a detailed empirical assessment of rates of progression through the HIV care cascade from an individual-level longitudinal data, this paper aims to quantify the extent to which the results change when models fail to incorporate a realistic understanding of the cascade.

2.4 Methods

This study is composed of two parts: a longitudinal data analysis from an empirical cascade of care, and the construction of two models, one that reflects the structure of the empirical cascade as well as the leakages and delays in receiving care, and another that reflects the conventional assumptions observed in published models. We compared the health benefits derived from the two models under different treatment eligibility thresholds, and estimated the incremental health benefits of increasing the threshold.

Study site and population

The Africa Health Research Institute (AHRI), located in KwaZulu-Natal, South Africa, has maintained an HIV-focused health and demographic surveillance system in the region since 2003, including individual HIV testing, annual household survey data, and clinical records. This region has a very high prevalence of HIV and poor socioeconomic indicators (16). Rates of reaching subsequent stages of the cascade were obtained through individually-linked longitudinal analysis (17) within the same population, avoiding concerns of double-counting the recurring patients as a separate individual and misclassifying deaths or those that sought

care at other locations as lost to follow up (LFU) (18). Detailed description of the data source is available elsewhere (16,17).

We identified 7,707 patients with records of first HIV-positive test results, which is recorded in the surveillance data and does not reflect the time of infection nor when they first learn their positive status, and followed them through their subsequent interactions with the health system. All dates in which patients accessed care, including whether they are aware of their positive status, enrolled in pre-ART care, and initiated ART, are recorded. Individuals were considered eligible for ART if they had a CD4 count that met the eligibility criteria, which varied over time. The eligibility threshold was CD4 count ≤200 cells/μL up to July 2011, and the threshold was raised to CD4 count ≤350 cells/μL afterwards during the study period. Every six months, pre-ART patients were scheduled to return to care to determine eligibility, and patients on ART were scheduled for follow-ups. If they did not return on expected dates, their LFU dates as well as return dates (if they return) were documented. Approximately half of the sample (n=3,533) had records of their CD4 count before or at the time of being linked to pre-ART care. Everyone was censored in January 2014. Detailed definitions of each health state and its associated activities are in Appendix S2.1.

Statistical analysis

We estimated time varying monthly probabilities of transition between cascade stages. Seven transitions were estimated: (1) from undiagnosed to diagnosed; (2) from diagnosed to linked to pre-ART care; (3) from retained in pre-ART care to LFU; (4) from LFU from pre-ART to returning to pre-ART care; (5) from pre-ART care to receiving ART; (6) from retained in ART to LFU; and (7) from LFU from ART to resumed ART. We describe the methods for deriving monthly transition probabilities for each transition in Table 2.1.

Model design

We developed two discrete-time Markov models, one reflecting the structure of the empirical cascade data and another of existing models, to compare the differences in the

estimated health benefits between the two models. The empirically-based cascade model includes 25 mutually exclusive health states, representing four CD4 count stages, four cascade stages, two lost-to-follow-up stages, and one absorbing state (death) (Figure 2.1). We applied the sets of transition probabilities along the treatment cascade described above. Model parameters related to the natural progression of and recovery from the disease and mortality were derived from published literature, listed in Appendix S2.2.

The second model reflects the optimistic assumptions commonly found in existing models. In this 'conventional' model, the cohort goes through the treatment stages with minimal leakages and time delays in being linked to care (6,7,9) (Figure 2.2). Nine health states were constructed, representing different CD4 count stages, treatment stages, and the absorbing state (death). When patients are diagnosed with HIV, their CD4 counts are checked to determine ART eligibility. Once their CD4 count drops below the eligibility criteria, they are immediately initiated on treatment, and throughout their lifetime experience low rates of dropouts (only 1.5 percent drop out every year) (6). Those who drop out return to treatment at the same rate as the treatment naïve patients.

Both models started with a hypothetical cohort of HIV patients with CD4 counts greater than 500 cells/μL, and modeled the transitions the cohort faces along the cascade. We set the transition cycle to one month. To ensure compatibility between the models, we standardized the proportion of people being linked to the health system at 86% within four years after their first positive HIV test, per empirical data, starting from the lowest CD4 level.

The main health outcomes of interest were HIV mortality and HIV transmission. HIV mortality was calculated by subtracting the sum of the sojourn time from all non-death health states from the time spent alive. We summarized effects of treatment on transmission in terms of the cumulative number of secondary infections transmitted per infected person, in view of the strong commitment by the South African government to reduce HIV

incidence by 50 percent in five years in their National Strategic Plan 2012-2016 (19). In order to reflect variation in transmission risks that depend on different types of sexual risk behavior, we derived two different measures of second transmission, corresponding to serial monogamy and random mixing among sero-discordant partnerships. In both cases, the measures represent the number of secondary infections that would occur for each infected case in a fully susceptible population caused by this cohort, which is also known as the basic reproduction number R_0. To compute secondary infections for the serial monogamy model, we used the approximation developed by Hollingsworth et al. (20), which accounts for transmission hazards at successive stages of infection, rates of partner change, and the duration of each health stage. To compute secondary infections for the random mixing model we multiplied the stage-specific transmission rates by the duration of each health stage. Details on the transmission calculations are provided in Appendix S2.3.

We compared the incremental benefits of expanding treatment eligibility from CD4 count 200 to 350, 350 to 500, and 500 cells/μL to treating everyone. The comparisons reflect both the retrospective experience of broadening eligibility and the prospective expectation of broadening the eligibility further to a universal test and treat approach.

We conducted one-way sensitivity analyses on all constant transition probabilities to examine the robustness of our results, and the results are presented in Appendix S2.4.

2.5 Results

Empirical measures of transitions in the care cascade

Among the overall sample, 55% of those being diagnosed transitioned to pre-ART care within four years of their first positive HIV test. Before July 2011 when treatment eligibility threshold in South Africa was CD4 200 cells/μL, among those with a CD4 record (n=1,947), 53, 73, 70, and 81% of people with CD4 of less than 200, 200-350, 350-500, and above 500 were LFU from pre-ART care. Among those with CD4 less than 200 cells/μL and was linked to pre-ART (n=1,248), 82% initiated ART, and no one with a higher CD4

count initiated ART. Among those who initiated ART (n=1,024), 28% were LFU during the study period. Between July 2011 and January 2014 when treatment eligibility threshold was CD4 350 cells/μL, among those with a CD4 record (n=379), 31, 44, 35, and 37% of people with CD4 of less than 200, 200-350, 350-500, and above 500 were LFU from pre-ART care. Among those with CD4 less than 200 and 200-350 cells/μL, 73% (n=119) and 71% (n=77) of initiated ART, and among them, 8 and 17% were LFU from ART, respectively (Table 2.2).

Estimated mortality and survivorship in empirical cascade model and conventional model

Under the empirical cascade model, life expectancy for a cohort of HIV patients with CD4 greater than 500 cells/μL was estimated to be 14.9, 17.0, 18.0, and 18.2 years under the treatment eligibility criteria of CD4 count 200, 350, 500 cells/μL and treating all HIV-positives, respectively. In comparison, life expectancy estimates under the conventional model given the four eligibility thresholds were 15.8, 18.8, 23.8, and 28.5 years (Figure 2.3a). Figure 2.4 shows the distribution of mortality by cascade stages estimated by each model. In the empirical model, the majority of deaths occur before pre-ART care, since more than half of the population stay in this stage without ever being linked to pre-ART care or initiating ART. Expansions of treatment eligibility lead to increases in the proportion of mortality occurring during treatment, reflecting risks of death from causes other than AIDS. Changes in the eligibility threshold have a more pronounced effect on the distribution of mortality in the conventional model, from 13% of deaths occurring in treated patients with eligibility at CD4 200 cells/μL to 71% when everyone is treated irrespective of CD4.

Estimated infections averted by treatment in empirical cascade model and conventional model

The numbers of estimated secondary infections transmitted by each primary infection were higher in the empirical cascade model than in the conventional model for both behavioral scenarios. Under the random mixing scenario, there would be an estimated 1.67, 1.55, 1.46, and 1.44 secondary infections per case under the four treatment eligibility criteria, respectively (Figure 2.3b). As shown in Figure 5, the majority of transmissions would occur

before the person is linked to pre-ART, and the proportion would increase with higher treatment thresholds. In comparison, the number of secondary infections per case would be 1.52, 1.29, 0.88, and 0.42 in the four different eligibility criteria, respectively, in the conventional model. Nearly all transmissions occur when patients are undiagnosed under most treatment thresholds. When treatment is available to everyone irrespective of CD4 count, 27% of transmissions occur among people on ART because the time spent being on treatment is much longer than not being on treatment. Under the serial monogamy scenario, the numbers of secondary infections per case were estimated at 1.08, 0.99, 0.92, and 0.90 in the empirical cascade model, and 1.03, 0.90, 0.65, and 0.29 in the conventional model, respectively (Figure 2.3c).

Incremental benefits from expanding treatment eligibility

Considering the benefits in moving from one eligibility criterion to the next, we estimated smaller health benefits with each expansion of treatment eligibility in the empirical cascade model compared to the conventional model, reflecting the impact of the cascade (Table 2.3), and the differences were especially pronounced as more inclusive eligibility criteria were adopted. In the empirical cascade model, raising the eligibility criteria from CD4 count 200 to 350 cells/μL increased population life expectancy by 25.9 months and reduced the average number of new infections caused by an individual by 0.11 and 0.09 for the two behavioral scenarios, respectively. The conventional model suggests greater health benefits: the policy change increased life expectancy by 36.5 months and reduced secondary infections by 0.23 and 0.13 for the two behavioral scenarios, respectively. Further expanding ART eligibility from CD4 350 to 500 cells/μL would increase life expectancy by 11.4 months in the empirical cascade model, compared to 60.0 months in the conventional model, with secondary infections declining by 0.09 and 0.07 for the two behavioral scenarios, compared to 0.41 and 0.25 in the conventional model. Finally, increasing the treatment threshold from CD4 500 cells/μL to treating everyone would add only 2.7 months of life expectancy in the empirical cascade model, compared to 56.0 months in the conventional model, and to reduce secondary infections modestly by 0.02 under both behavioral scenarios, compared to 0.46 and 0.36 in the conventional model.

Comparing the two models in relative terms, the conventional model produces estimated increases in health outcomes (both life years gained and transmission averted) that are roughly twice as great as those in the empirical cascade model under an eligibility expansion from CD4 count 200 to 350 cells/μL, three to five times higher with a change from 350 to 500 cells/μL, and 15 to 21 times higher with the expansion from 500 cells/μL to treating everyone. The ratio is much larger in the latter policy scenario because of the relatively smaller incremental benefits estimated in the empirical cascade model with eligibility threshold expansion.

2.6 Discussion

This study showed that existing models that do not account for the delays and leakages in the continuum of HIV care may be overestimating the health benefits gained from these policy changes by a substantial multiple. In the case of raising the HIV treatment eligibility threshold from CD4 200 to 350 and 350 to 500 cells/μL, years of life gained and HIV transmission averted by this policy change may be overestimated by approximately two to five-fold. In the case of raising the HIV treatment eligibility threshold from CD4 500 cells/μL to treating everyone irrespective of their CD4 count, health benefits gained from this policy change may be overestimated by approximately 15 to 21-fold.

The findings of this paper have major policy implications. The latest World Health Organization guideline recommends ART to be initiated in everyone living with HIV at any CD4 count (21), and evidence on the incremental health benefits or cost-effectiveness of expanding from one treatment eligibility criterion to another are needed to make decisions. However, overestimating health benefits of eligibility expansion policies may lead to inefficient resource allocation and program planning. Many conventional models implicitly assume that the targets of achieving high linkage, high retention, and minimal delays can be achieved for free, requiring no additional resources (5–9). For example, by applying a HIV testing rate of 90 percent (6), the model are assuming that no additional investments for outreach programs are needed to increase testing rates from baseline, which is often much

lower than 90 percent. We argue that the models should either reflect the leakages and delays in the treatment cascade, which will reduce the estimated incremental health benefits, or assign costs that are associated with programs that have demonstrated effectiveness in increasing of testing (22), linkage (23), and adherence rates (24,25), which will increase costs. Linking these conventional health benefits to unrealistic costs will lead to an overestimation of the cost-effectiveness of the interventions, further leading to suboptimal budgetary decisions made by the consumers of the information.

Our study has several limitations. First, there are limits to the generalizability of the specific numerical findings from the AHRI to other settings, including its high HIV prevalence observed in a rural sub-Saharan African population. However, the HIV treatment cascade has been reported in many diverse settings, thus we believe that the main conclusion of this paper, namely that health benefits attributed to changes in treatment eligibility is largely overestimated, is applicable beyond this study population. Second, we intentionally created a simplistic model with straightforward computations to devise heuristics regarding the potential magnitude of cascade effects on HIV transmission and mortality. The way in which we estimate the effect of the treatment cascade on HIV incidence and mortality are crude methods, which limit our results to two summary outcomes of benefit, whereas more sophisticated models allow or more details characterizations of the dynamics of evolving epidemics and estimation of a broader range of outcomes. However, we believe the conventional model in this study appropriately reflects the commonly applied assumptions used in published literature. For example, the estimated percentage reductions in secondary transmission from increasing eligibility from CD4 350 to 500 cells/μL, and to treating everyone irrespective of their CD4 count are comparable to what has been published (5–7). Third, the Markovian assumption – i.e. that the probability of moving between states in the model is not dependent on the states a patient may have experienced before entering that state – is an important limitation of this model, as it is in many other models. In HIV, patients, those who were linked to pre-ART care longer may be more likely to be adherent when they receive ART, or those that were LFU at some point may have a higher probability of becoming lost again. Finally, we acknowledge that accurate estimation of both costs and health effects are critical in generating a useful cost-effectiveness study. Due to lack of data

we do not explore how the cost of implementing HIV care programs is impacted by the treatment cascade.

The need for modeling studies to inform decisions regarding alternative policy scenarios will persist as the global public health community continues to advance towards goals for HIV elimination. This paper aims to facilitate better decision making by highlighting the importance of capturing the empirical realities of the care cascade in HIV models and quantifying the magnitude of overestimation of health benefits from policy changes when analyses fail to include an accurate accounting for these factors.

2.7 References

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2.8 Main Figures and Tables

Table 2.1. Methods for deriving transition probabilities for between cascade stages

	Transition	Method
(1)	Undiagnosed to diagnosed	• Estimated the proportion of the full sample who were diagnosed within four years after their first positive HIV test • Calculated the monthly transition probability required to achieve that proportion by first setting 86% of individuals with CD4 count less than 200 cells/μL to be diagnosed within four years and derived the monthly probability needed to meet this requirement. Conditioning on this probability, we then fixed 86% of individuals with CD4 count below 350 cells/μL to be diagnosed within four years, and continued the same approach for individuals with CD4 count 500 and above 500 cells/μL
(2)	Diagnosed to linked to pre-ART care	• Estimated monthly transition probability by applying Kaplan-Meier non-parametric survival analysis on the full dataset, pooled across CD4 levels
(3)	Retained in pre-ART care to LFU	
(4)	LFU from pre-ART to returning	
(5)	Pre-ART care to receiving ART	• Estimated monthly transition probability by applying Kaplan-Meier non-parametric survival analysis on the full dataset, stratified by CD4 cell count at time of linkage to pre-ART care • Under the eligibility criterion of CD4 count below 200 cells/μL, we estimated the transition probability among people who were linked to pre-ART care before July 2011 and applied the non-parametric probabilities to each CD4 category • Under the eligibility criterion of CD4 count below 350 cells/μL, we estimated the probabilities among people who were linked to pre-ART care after July 2011 for each CD4 group • To approximate the rates of the higher CD4 groups under higher eligibility criteria, we calculated the hazard ratio of the Kaplan-Meier curves between the groups with CD4 count below 200 cells/μL and 200-350 cells/μL, and applied this hazard ratio to the rates of the group with 200-350 cells/μL to derive the rates for the CD4 group 350-500 cells/μL. We applied the same approach to derive the rates for the group with CD4 greater than 500 cells/μL
(6)	Retained in ART to LFU	• Estimated monthly transition probability by applying Kaplan-Meier non-parametric survival analysis on the full dataset, stratified by CD4 cell count at time of linkage to pre-ART care, under eligibility criteria of CD4 count below 200 and 350 cells/μL, respectively • For higher eligibility scenarios, we assumed that people experienced the same rates under the CD4 count below 350 cells/μL eligibility criterion
(7)	LFU from ART to resuming ART	

Table 2.2. Descriptive statistics of the HIV care cascade

		Proportion of people who transitioned to the next stage among those who reached the previous stage			
	Observed time period	CD4 >500 cells/μL	CD4 350-500 cells/μL	CD4 200-350 cells/μL	CD4 <200 cells/μL
Diagnosed → pre-ART	Jan 2004 - Jan 2014	55 %			
Pre-ART → loss to follow up under treatment threshold CD4 <200 cells/μL	Jan 2004 - Jul 2011	81 %	70 %	73 %	53 %
Pre-ART → loss to follow up under treatment threshold CD4 <350 cells/μL*	Aug 2011- Jan 2014	37 %	35 %	44 %	31 %
Pre-ART → ART initiation, under treatment threshold CD4 <200 cells/μL	Jan 2004 - Jul 2011	0 %	0 %	0 %	82 %
Pre-ART → ART initiation, under treatment threshold CD4 <350 cells/μL	Aug 2011- Jan 2014	0 %	0 %	71 %	73 %
ART care → loss to follow up under treatment threshold CD4 <200 cells/μL	Jan 2004 - Jul 2011	0 %	0 %	0 %	28 %
ART care → loss to follow up under treatment threshold CD4 <350 cells/μL	Aug 2011- Jan 2014	0 %	0 %	17 %	8 %

ART: antiretroviral treatment

Table 2.3. Incremental benefits of changing treatment eligibility

		Incremental benefit of eligibility change from CD4 200 to 350	Ratio of incremental benefits, optimistic to cascade	Incremental benefit of eligibility change from CD4 350 to 500	Ratio of incremental benefits, optimistic to cascade	Incremental benefit of eligibility change from CD4 500 to treat all	Ratio of incremental benefits, optimistic to cascade
Life expectancy (months)	Optimistic	36.5	1.41	60.0	5.27	56.0	20.7
	Cascade	25.9		11.4		2.7	
HIV transmission (random mixing)	Optimistic	0.23	2.02	0.41	4.50	0.46	19.7
	Cascade	0.11		0.09		0.02	
HIV transmission (serial monogamy)	Optimistic	0.13	1.46	0.25	3.59	0.36	15.3
	Cascade	0.09		0.07		0.02	

Figure 2.1. Schematic view of the cascade model

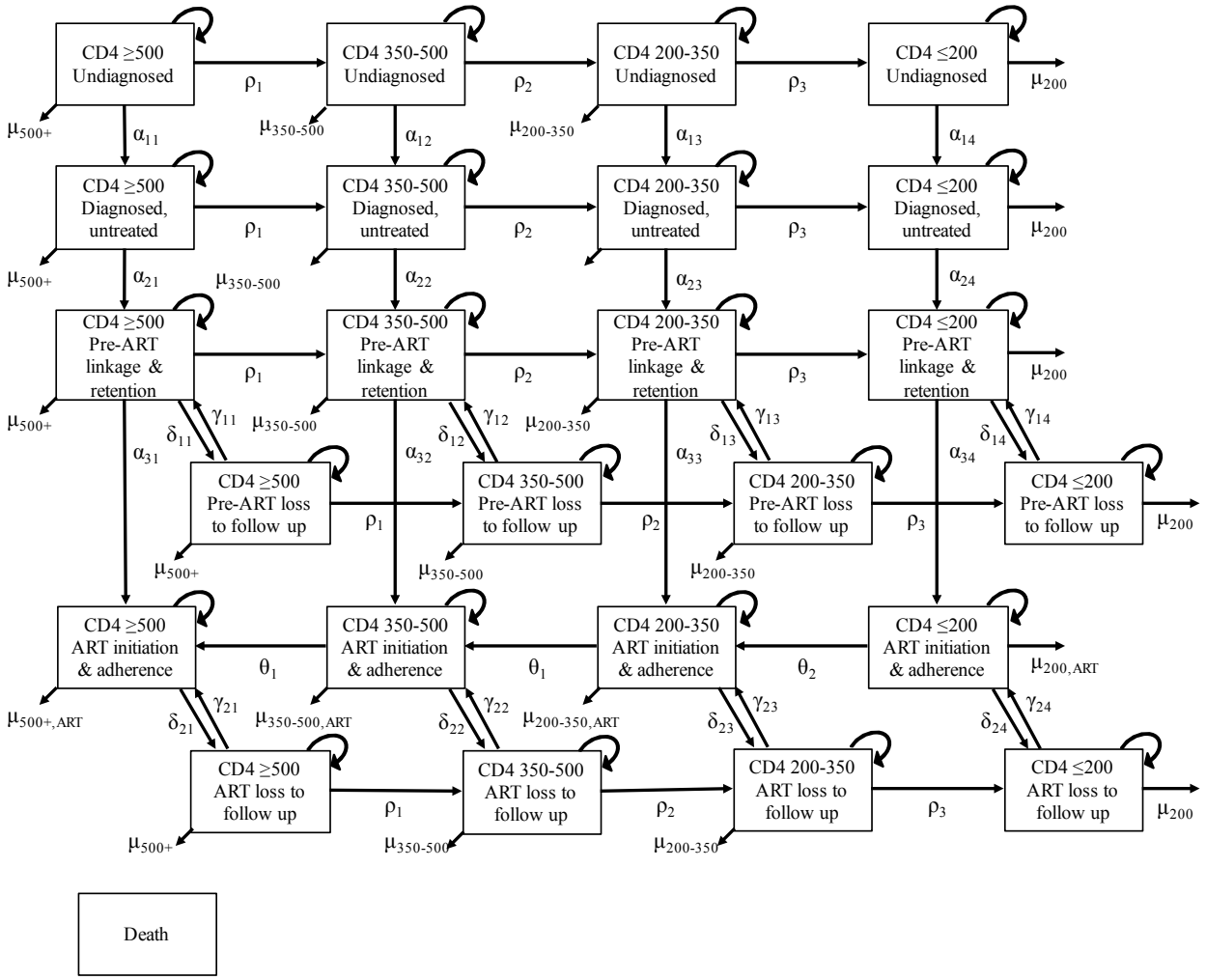


Figure 2.2. Schematic view of the optimistic model

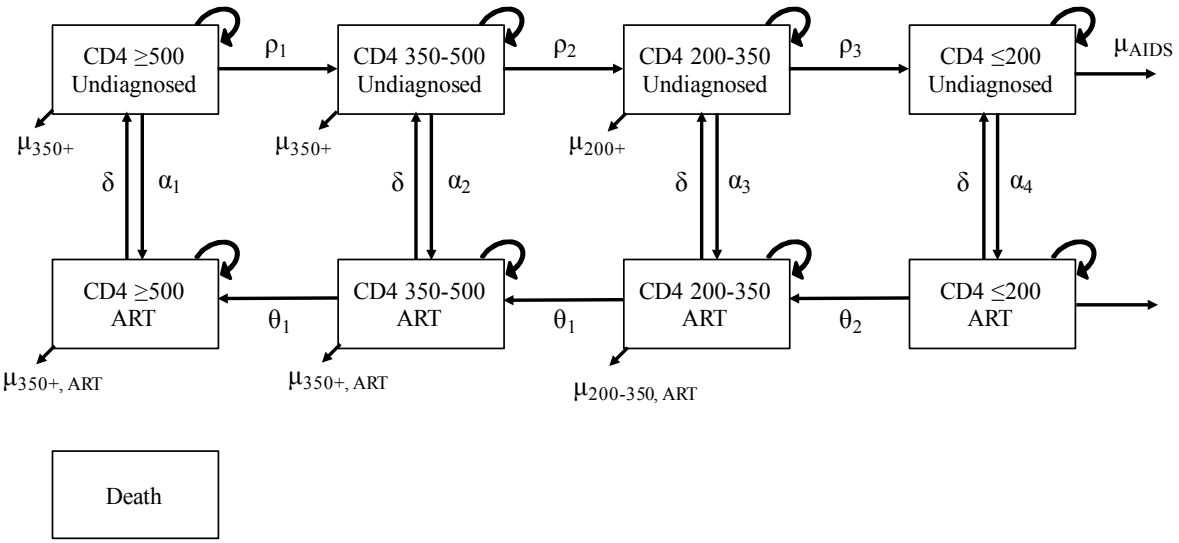
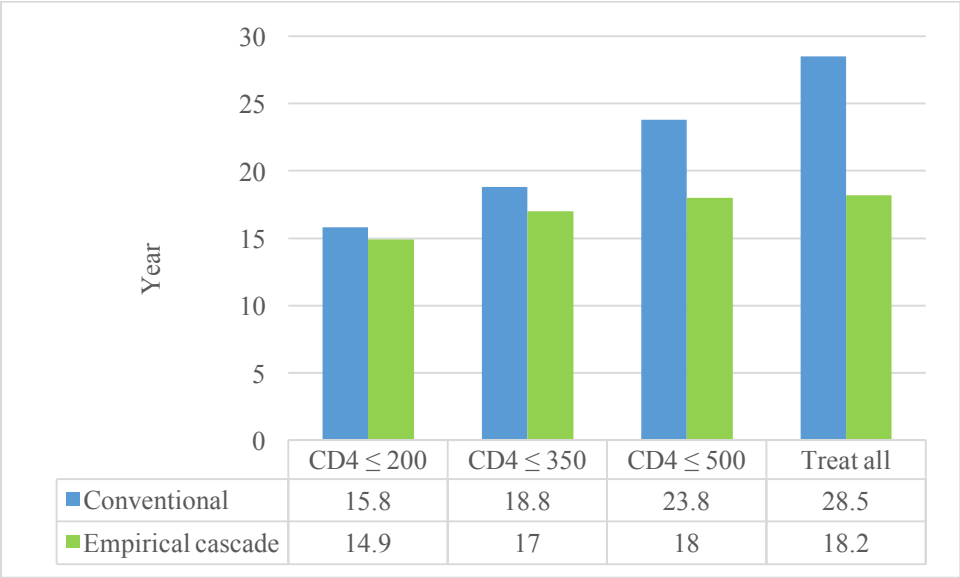


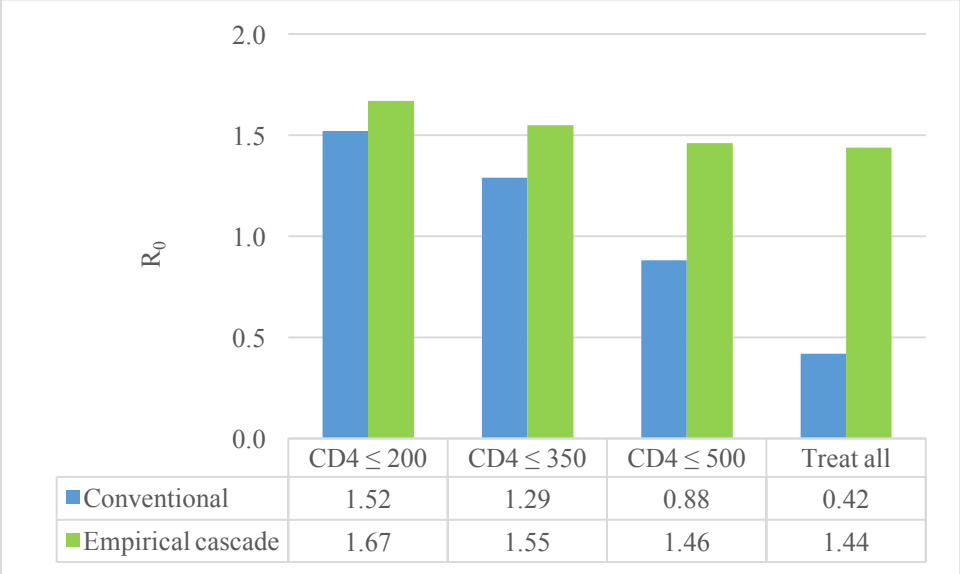
Figure 2.3a-c. Comparison of health benefits under the conventional and empirical cascade models, by treatment eligibility

3a. Life expectancy



	CD4 ≤ 200	CD4 ≤ 350	CD4 ≤ 500	Treat all
Conventional	15.8	18.8	23.8	28.5
Empirical cascade	14.9	17	18	18.2

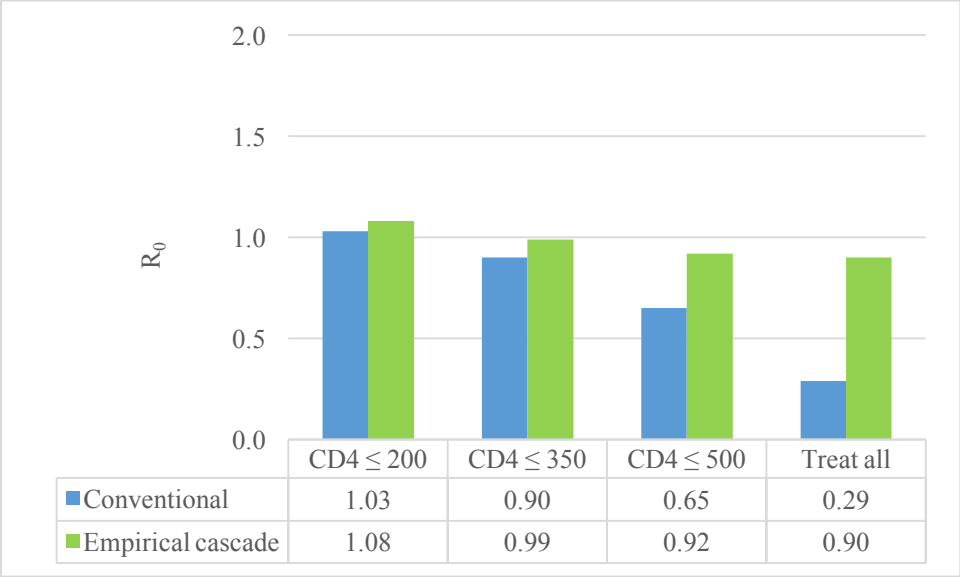
3b. Secondary transmission under random mixing scenario



	CD4 ≤ 200	CD4 ≤ 350	CD4 ≤ 500	Treat all
Conventional	1.52	1.29	0.88	0.42
Empirical cascade	1.67	1.55	1.46	1.44

R_0: basic reproduction number

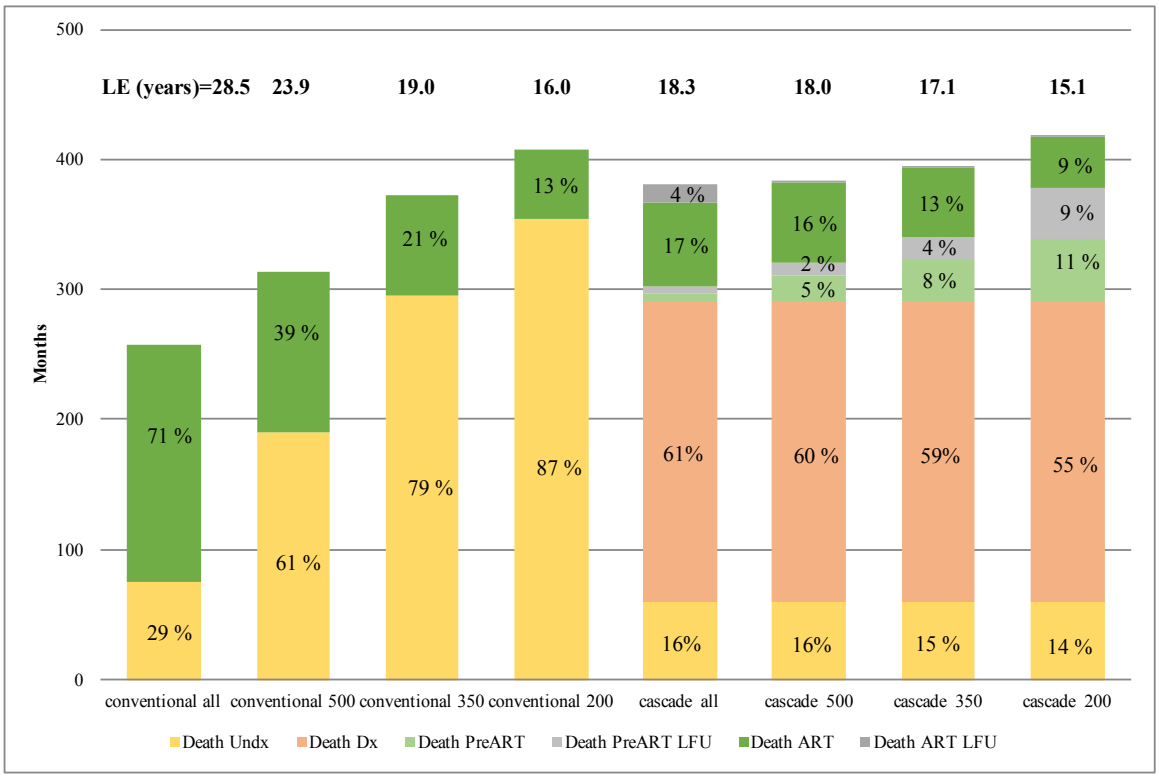
3c. Secondary transmission under serial monogamy scenario



	CD4 ≤ 200	CD4 ≤ 350	CD4 ≤ 500	Treat all
Conventional	1.03	0.90	0.65	0.29
Empirical cascade	1.08	0.99	0.92	0.90

R_0: basic reproduction number

Figure 2.4. Distribution of mortality by cascade stages

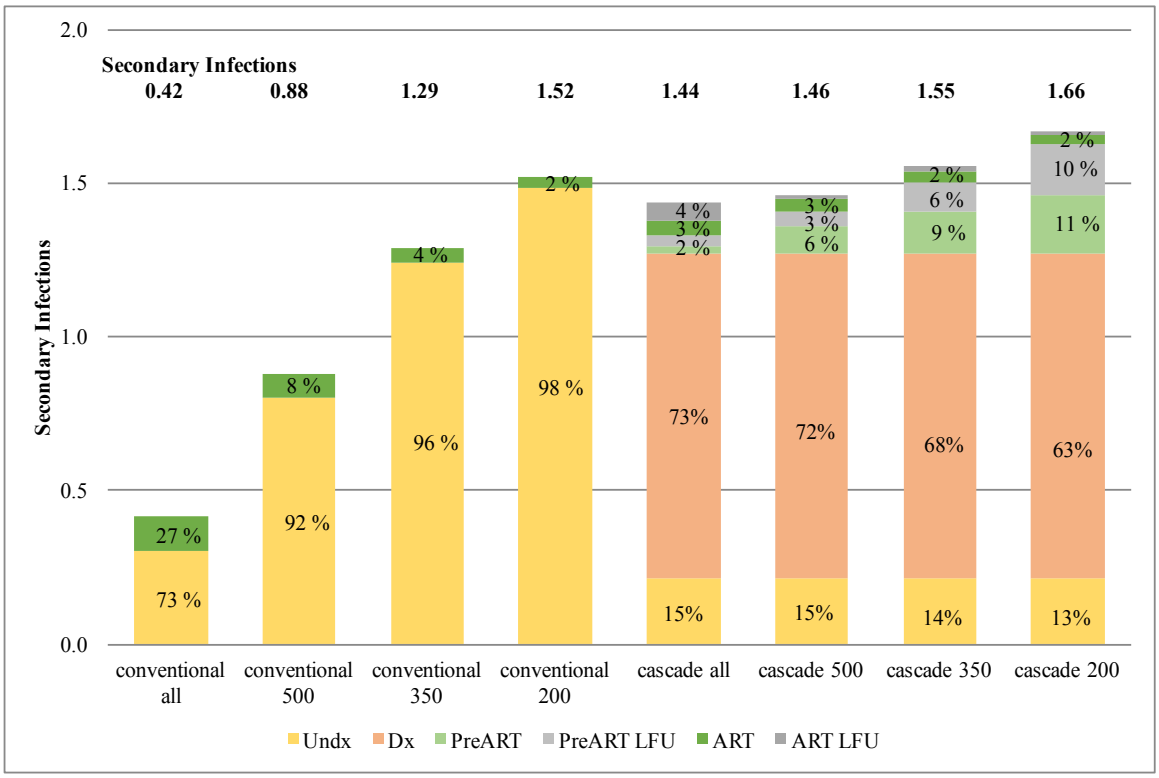


Undx: undiagnosed, Dx: diagnosed, ART: antiretroviral therapy, LE: life expectancy, LFU: lost to follow up.

conventional all/500/350/200: the conventional model with treatment threshold of treating everyone, CD4 count 500, 350, 200 cells/μL.

cascade all/500/350/200: the empirical cascade model with treatment threshold of treating everyone, CD4 count 500, 350, 200 cells/μL.

Figure 2.5. Distribution of HIV transmission (random mixing) by cascade stages



Undx: undiagnosed, Dx: diagnosed, ART: antiretroviral therapy, LE: life expectancy, LFU: lost to follow up.

conventional all/500/350/200: the conventional model with treatment threshold of treating everyone, CD4 count 500, 350, 200 cells/μL.

cascade all/500/350/200: the empirical cascade model with treatment threshold of treating everyone, CD4 count 500, 350, 200 cells/μL.

2.9 Supplemental Material

S2.1. Definition of each health state and its associated activities

The following definitions of health states and the activities associated with each state are defined by the Africa Centre (1):

- Diagnosed with HIV: We define individuals in this state as those who knows his/her positive HIV status after their first positive test.
- Pre-ART care linkage and retention: Individuals are considered linked to pre-ART care if they have a recorded HIV clinic visit, registration at a clinic, CD4 test, viral load count, or initiated ART. At the initial HIV diagnosis, providers are expected to check their CD4 count on the same day, although in reality this is rarely done. They are then expected to return for a repeat CD4 count and WHO clinical staging every six months to see if they have become eligible for ART. We define individuals who are retained in pre-ART care as those who have an assessment every six months and were not ART eligible at the last assessment. They are considered lost to follow up if they do not return to receive pre-ART services within six months since their last visit.
- ART initiation and adherence: Individuals are recorded as having initiated ART based on the records of the date of the first ART prescription. During the study period, South Africa's ART eligibility criterion shifted from the initial CD4 count of 200 to 350 cells/mm^3 in July 2011.

S2.2. Model parameters related to the natural progression of and recovery from the disease

Table S2.1. Model parameters related to the natural progression of and recovery from the disease

Model parameter	Value	Data source
Monthly probability of progression to the next disease stage, without ART (month^{-1})	CD4 >500: 0.0161 CD4 350-500: 0.0298 CD4 200-350: 0.0189	(2)
Monthly probability of CD4 recovery when under treatment (month^{-1})	CD4 350-500: 0.1823 CD4 200-350: 0.1823 CD4≤200: 0.1122	(3)
Monthly probability of mortality, without ART (month^{-1})	CD4 > 500: 0.0038 CD4 350-500: 0.0038 CD4 200-350: 0.0067 CD4≤200 : 0.0225	(4)
Monthly probability of mortality, with ART (month^{-1})	CD4 > 500: 0.0010 CD4 350-500: 0.0017 CD4 200-350: 0.0021 CD4≤200: 0.0129	(5)
Baseline mortality rate (month^{-1})	Varies by year	(6)

S2.3. Cumulative number of secondary HIV infections and HIV infectiousness for each health stage

Cumulative number of secondary HIV infections

In a serial monogamous population, the expected number of infections was computed based on an approximation formula developed by Hollingsworth et al. (7):

$$R_0 = \sum_{ij} \frac{\beta_{ij} c d_{ij}}{\beta_{ij} + c + \frac{1}{d_{ij}}} \quad (1)$$

where β_{ij} is the transmission hazard for health stages (i: cascade health states, j: CD4 levels), c is partner change rate (set at 1.25 per year), and d_{ij} is the duration of the health stage. Hollingsworth et al. provide the hazard rates of HIV transmission by each infection stage (7). The contribution to the number of new infections in a fully susceptible population caused by this cohort, also known as the basic reproduction number R_0, is therefore the probability of transmission $\frac{\beta_{ij} c d_{ij}}{\beta_{ij} + c + \frac{1}{d_{ij}}}$, multiplied by the rate of partner change c, and the duration of the health state d_{ij}.

Three possible outcomes may occur once a discordant partnership is formed: the partnership may discontinue with hazard c; the infected partner may progress to the next stage of disease with hazard $1/d_{ij}$, where d_{ij} is the duration of the stage of infection; or transmission may occur with hazard β_{ij}. Thus, the probability of transmission to a partner in this stage of the infection may therefore be approximated by $\frac{\beta_{ij} c d_{ij}}{\beta_{ij} + c + \frac{1}{d_{ij}}}$.

In a random mixing population, the expected number of infections was computed as:

$$R_0 = \sum_{ij} \beta_{ij} d_{ij} \quad (2)$$

which is the transmission rate multiplied by the duration of each health stage.

HIV infectiousness for each health stage

Hollingsworth et al. provide the hazard rates of HIV transmission by each infection stage (Table S2.2) (7). We set the transmission hazard for patients with CD4 count greater than 200 cells/mm^3 equal to the rate for the asymptomatic infection stage, and the rate for patients with CD4 count less than 200 cells/mm^3 equal to the rate for the patients 10-19 months before death. Transmission hazard for those on ART are reduced by 96% (8).

Table S2.2. HIV infectiousness for each health stage

Treatment status	Health stage	Monthly HIV transmission hazard	Reference
Not on ART	CD4 500+	0.0088	(7)
	CD4 350-500	0.0088	
	CD4 200-350	0.0088	
	CD4 <200	0.0633	
On ART	CD4 350+	0.00035	(7,8)
	CD4 200-350	0.00035	
	CD4 <200	0.00253	

S2.4. Sensitivity analyses

We conducted one-way sensitivity analyses on all constant transition probabilities to examine the robustness of our results. The baseline values for each parameter were increased or decreased by 50 percent, and we record variables for which the change in the parameter led to a change in the ratio of incremental benefits of greater than 25 percent in Table S2.3.

None of the parameter changes resulted in large changes under the threshold expansion from CD4 200 to 350 cells/mm^3. Under the threshold expansion from CD4 350 to 500 cells/mm^3, the main result was only sensitive to one parameter, the rate of disease progression from CD4 350-500 to CD4 200-350 cells/mm^3. Under the threshold expansion from CD4 500 cells/mm^3 to all HIV positives, the main result was sensitive to the rate of disease progression from CD4 200-350 to CD4 dropping below 200 cells/mm^3 and the mortality rate for those with CD4 greater than 500 cells/mm^3 when not on treatment. Natural disease progression and mortality rates were derived from published literature, and it is unlikely that these parameters are over- or underestimated by 50 percent. In the scenario of increasing treatment eligibility from CD4 500 cells/mm^3 to all HIV positives, the range of the ratio is much wider because the denominator of the ratio (health benefits gained in the cascade model) is relatively small compared to other policy scenarios.

Table S2.3. Sensitivity analyses results for estimated life expectancy

Eligibility change from CD4 350 to 500			Eligibility change from CD4 500 to all HIV+		
Parameter	Ratio of incremental benefits between optimistic and cascade models, life expectancy (% change from the main result, 5.27)		Parameter	Ratio of incremental benefits between optimistic and cascade models, life expectancy (% change from the main result, 20.8)	
Parameter range	+50%	-50%	Parameter range	+50%	-50%
Progression from CD4 350-500 to CD4 200-350 cells/mm^3	6.27 (+19%)	**3.72 (-29%)**	Progression from CD4 200-350 to CD4≤200 cells/mm^3	**32.51 (+256%)**	**5.48 (-74%)**
			Mortality rate for CD4 ≥ 500 cells/mm^3 without treatment	21.02 (+1%)	**31.63 (+52%)**

* Results with difference from the main result of greater than 25 percent are presented in bold

S2.5. References

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Chapter 3. The effect of concordant and discordant diseases on progression in the care continuum for hypertension, diabetes, and HIV among older adults with multimorbidity in Agincourt, South Africa

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3.1 Abstract

Background

The rapid aging of populations in low- and middle-income countries has given rise to the prevalence of multimorbidity. This study assessed how the types of multimorbidity (concordant versus discordant) affects a patient's progression along the care continuum for hypertension, diabetes, and HIV in rural South Africa.

Methods

We analyzed cross-sectional data of 4,447 people age 40 and above enrolled in the Health and Aging in Africa: A longitudinal study of an INDEPTH Community in South Africa (HAALSI) program. For hypertension and diabetes, we considered persons to have concordant multimorbidity if they had other cardiometabolic diseases, and to have discordant multimorbidity if they had mental disorders or HIV infection. For HIV infected patients, any other diseases were considered discordant. Regression models were fitted to assess the relationship between the likelihood of being in each care stage for the index disease and the type of multimorbidity.

Results

People with hypertension or diabetes with concordant cardiometabolic diseases were more likely to proceed further along the continuum-of-care (hypertension 0.33 additional stages, 95%CI 0.23-0.44; diabetes 1.30, 95%CI 0.79-1.82). Having discordant diseases was associated with further progression in care for hypertensive people (mental disorder 0.25, 95%CI 0.12-0.38; HIV 0.19; 95%CI 0.04-0.33) but not for diabetics. For HIV patients, having discordant cardiometabolic conditions was associated with less progression in HIV care (-0.35, 95%CI -0.54 – -0.11). Looking at each stage of the continuum, having concordant multimorbidity was associated with higher likelihood of being diagnosed (OR=1.53, 95%CI 1.24-1.88), initiated treatment (OR=1.52, 95%CI 1.21-1.92), and currently being on treatment (OR=1.46, 95%CI 1.08-1.97) for hypertension. Having discordant mental disorders increased the likelihood of being in the earlier stages of care for people with hypertension (OR=1.52, 95%CI 1.17-1.99). Among those with diabetes, having concordant multimorbidity increased the odds of knowing their diabetes status (OR=4.20, 95%CI 2.19-8.19). Individuals with HIV and discordant cardiometabolic diseases received worse HIV care: 54% lower

odds (OR=0.46, 95%CI 0.30-0.69) for knowing their HIV status, and 68% lower odds (OR=0.32, 95%CI 0.09-0.87) for ever receiving antiretroviral treatment.

Conclusions

The type of multimorbidity is associated with one's progression along the continuum-of-care, and the care stages with lower opportunity costs benefit from the presence of any type of comorbidity, while stages with higher opportunity costs only benefit from concordant conditions. In populations with high prevalence of multimorbidity, more nuanced interpretation of the effect of the types of multimorbidity on a person's progression along the care continuum should be incorporated in the design of the healthcare delivery system.

Funding

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3.2 Keywords

Multimorbidity, concordance, hypertension, diabetes, HIV, aging, cascade of care

3.3 Introduction

The rapid aging of populations in low- and middle-income countries (LMICs) has given rise to the increased prevalence of multimorbidity, commonly defined as persons with more than one clinical condition (1). Previous studies have found that multimorbidity is associated with poorer clinical outcomes (2), higher health expenditure and frequency of service utilization (3–6), higher use of secondary care compared to primary care (7,8), and higher hospitalization rates (3,6,9).

One limitation in the existing literature is that equal weights are assigned to all comorbidities. However, it is reasonable to assume that different combinations of diseases affect the person's health and healthcare differently. To account for these differences, in this paper, we categorize multimorbidity into those with concordant or discordant diseases. Piette and Kerr (10) defined concordant diseases as those with similar pathophysiologic risk profile with similar management plans, and discordant diseases as those that are not directly related in either their pathogenesis or management. Both theoretical and empirical literature in high-income settings have explored the effect of the specific types or combinations of diseases on one's progression along the care continuum, here defined as progressing through the typical stages of care, such as being tested for the disease, being aware of the diagnosis, and receiving appropriate treatment. Theoretically, concordant diseases are more likely to be diagnosed and treated along with the index disease because clinical guidelines often incorporate their interactions. For discordant diseases, the competing demands model suggests that providers face several competing demands during the medical encounter, which may lead them to provide lower quality of care (11). On the patient side, any additional condition, especially those that impair functioning, poses further time and energy requirements. Empirical evidence in high-income countries show that patients with concordant conditions had higher odds of achieving testing and control goals for the index disease compared with those with discordant diseases. This is true for diabetes in the U.S. (12,13) and hypertension in U.S. and Mexico (14,15). Diabetes patients with discordant diseases, on the other hand, were found to have higher unplanned hospital service use and specialized care use than those with concordant diseases in Spain (16). Little is known about HIV/AIDS care among patients with HIV with multimorbidity, although studies did find that patients with HIV in the U.S. receive poorer care than those without HIV for their coexisting conditions (17–19).

Much less is known about how the type of multimorbidity (concordant or discordant) affects one's progression along the continuum-of-care in LMICs, and especially in sub-Saharan Africa. Our study aims to fill this significant knowledge gap by studying the progression along the care continuum among people with one of the three diseases of interest: hypertension, diabetes, and HIV – all prominent conditions contributing to sub-Saharan Africa's complex health transition. Furthermore, this study is one of the first to assess the effect of the type of multimorbidity on HIV care among HIV patients. We hypothesized that among people with the index disease, people with concordant multimorbidity progress further along the continuum for the index disease, and those with discordant multimorbidity progress less.

3.4 Methods

Study design, participants, and setting

The "Health and Aging in Africa: A longitudinal study of an INDEPTH Community in South Africa" (HAALSI) study is a cross-sectional study conducted in the Medical Research Council/Wits Agincourt Health and Demographic Surveillance System site in the sub-district of Agincourt, in the Bushbuckridge area of Mpumalanga Province in South Africa (20). This population-based survey enrolled 5,059 participants age 40 and above. Household-based interviews were completed between November 2014 and November 2015 with a primary survey instrument querying the demographics, health and economic conditions of all participants. More details on data collection are described elsewhere (21).

The Agincourt sub-district has six clinics and two health centers, and three district hospitals located between 25 and 60 km from the study site (20,22). Primary health care services are free of charge, and the majority of health expenditures are spent on transportation fees, caregiver costs, or private services. The Integrated Chronic Disease Management (ICDM) model was recently introduced in South Africa to address several crucial elements in managing multimorbidity, including standardized clinical care based on national treatment protocols and promotion of disease monitoring and management among patients (23–25). In the context of Agincourt, under ICDM, a patient with any symptom or disease arriving at a local clinic will be received by a nurse who is expected to address all

patient needs. Those seeking HIV testing will follow a separate process and only if they are diagnosed as HIV positive will they be referred to follow the same process along with other patients.

Disease and care status of the index diseases (hypertension, diabetes, and HIV), and selection of concordant and discordant diseases

The three "index" conditions are in reference to the care continuum the regression model is assessing, and not about its time sequence of occurrence or diagnosis. For example, hypertension is the index condition when the model is assessing the progression in the hypertension care. Hypertension was defined as either a mean systolic blood pressure of at least 140 mmHg, mean diastolic blood pressure of at least 90 mmHg, or self-report of current treatment. Diabetes was defined as either having glucose ≥126 mg/dL in fasting group (defined as >8 hours), glucose ≥200 mg/dL in nonfasting samples, or self-report of current treatment. HIV status was ascertained either from the collected dried blood spots (DBS) that showed HIV infection or exposure to antiretroviral treatment (ART), or self-report of disease status.

In addition to the three index diseases, five others were selected as concordant or discordant diseases: dyslipidemia, angina, depression, post-traumatic stress disorder (PTSD), and alcohol dependence. The disease statuses of these conditions were ascertained based on clinical diagnosis or clear clinical criteria, described further in Appendix S3.1. To determine concordance and discordance, we relied on the South African national guidelines to see which risk factors and comorbidities they consider in diagnosing and treating the index diseases (26,27). For hypertensive patients, we categorized those with dyslipidemia, diabetes, and/or angina as having concordant diseases, and those with any of the remaining diseases as discordant. Similarly, for diabetic patients, those with hypertension, dyslipidemia, and/or angina were classified as having concordant diseases, and those with additional remaining diseases as having discordant diseases. For people with HIV, we considered those with any of the other selected diseases as discordant.

Continuum-of-care was defined to include the sequential stages of care: test, diagnosis, ever being initiated on treatment, and currently retained on treatment. For hypertension and diabetes, whether a person reached each stage was determined by the self-reported status of reaching the stage. For

HIV, we relied on both self-reported status and results of the blood sample to determine progression. Those with DBS results that showed ART exposure were considered to have reached the treatment stage and all preceding stages, even if they self-reported otherwise.

Statistical analyses

We developed descriptive analyses of the prevalence of the three index diseases as well as the prevalence of concordant and discordant diseases by key sociodemographic covariates. We measured how far along the continuum-of-care people progressed, creating a continuous variable that added up the stages the individual completed, with the highest possible number set at four. Linear regression models were fitted to analyze the relationship between the number of steps one reached in the continuum-of-care and the type of multimorbidity.

Logistic regression was applied to obtain the odds ratio and 95% confidence interval for the relationship between the likelihood of being tested for the index disease and the type of multimorbidity among the entire sample and those with the index disease. We then explored the likelihood of getting to each stage in the continuum, conditional on having the index disease and reaching all previous stages, adjusting for sociodemographic covariates. Covariates included in the analyses are age, sex, education, country of origin, marital status, household size, employment status, having limitations in activities of daily living (ADLs) (as a proxy for health status), and wealth, measured in quintiles based on household asset ownership, and synthesized using standard methods (28).

All analyses were conducted in R software version 3.3.1 (29).

Ethics statement

The study received ethical approvals from the University of the Witwatersrand Human Research Ethics Committee, the Mpumalanga Provincial Research and Ethics Committee, and the Harvard T.H. Chan School of Public Health Office of Human Research Administration.

Role of the funding source

The funder had no role in the study design, data collection, data analysis, data interpretation, or writing of the report, or the decision to submit for publication. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

3.5 Results

We had full disease and continuum-of-care data on 4,447 (88%) of the whole sample. Table 3.1 shows the prevalence of hypertension (56%), diabetes (10%) and HIV (20%) by sociodemographic covariates, as well as the prevalence of concordant and discordant diseases. Among those with hypertension, 55% presented with one or more additional cardiometabolic condition, 22% with one or more mental disorders, and 17% with HIV. Among those with diabetes, 91% has other cardiometabolic conditions, 27% mental disorders, and 15% HIV. Among those with HIV, 71% presented with cardiometabolic conditions and 18% with mental disorders. Reflecting the wider population profile, people with HIV were, on average, younger, poorer, separated/deserted from partners and more likely to be employed compared to those with hypertension and diabetes.

Comparing across the continuum-of-care of the three index diseases, people with hypertension (0.33 additional stages; 95%CI 0.23-0.44) or diabetes (1.30; 95%CI 0.79-1.82) with one or more concordant cardiometabolic diseases were more likely to proceed further along the continuum-of-care, compared to those with just hypertension or diabetes alone (Table 3.2). In other words, having one or more concordant diseases was associated with better progression in hypertension and diabetes care than those with no concordant diseases. In contrast, having discordant diseases was associated with further progression in care for hypertensive people (mental disorders 0.25; 95%CI 0.12-0.38; HIV 0.19; 95%CI 0.04-0.33) but not for diabetics. Other covariates that were associated with the progression of care among people with hypertension included being older, female, having limitations in ADLs, of South African origin, and wealthier. For HIV patients, having discordant cardiometabolic conditions was associated with less progression in HIV care (-0.33, 95%CI -0.54 – -0.11), compared to people with only HIV and no cardiometabolic conditions. Other covariates that were associated with the further progression of care included being older, male, and living in larger households.

Looking more closely at each stage of the continuum, having discordant diseases was associated with higher likelihood of testing for hypertension, both among the entire sample population (mental disorders OR=1.32, 95%CI 1.11-1.57; HIV OR=1.20, 95%CI 1.02-1.42) and those with hypertension (mental disorders OR=1.44, 95%CI 1.15-1.82; HIV 1.29, 95%CI 1.01-1.65) (Table 3.3). Having discordant mental disorders was also associated with higher likelihood of a hypertensive patient being diagnosed for hypertension (OR=1.52, 95%CI 1.17-1.99), but was not associated with any of the succeeding stages in the continuum-of-care. Having HIV was not associated with the likelihood of being in any of the stages among hypertensive patients. In comparison, having one or more concordant cardiometabolic diseases was associated with higher likelihood of being diagnosed (OR=1.53, 95%CI 1.24-1.88), ever treated (OR=1.52, 95%CI 1.21-1.92), and currently on treatment (OR=1.46, 95%CI 1.08-1.97) for hypertension.

The effects of the types of multimorbidity on diabetic patients were greater. Having concordant cardiometabolic conditions was associated with higher odds of testing for diabetes both among the general population (OR=1.75, 95%CI 1.51-2.04) and those with diabetes (OR=4.20, 95%CI 2.19-8.19). Among those with diabetes, having concordant diseases was associated with higher odds of knowing their diabetes status (OR=3.55, 95%CI 1.34-9.64) but not for initiating or retaining in treatment. Having discordant diseases was not associated with progression to each stage. In contrast, among individuals with HIV, having discordant cardiometabolic diseases was associated with worse HIV care: 54% lower odds (OR=0.46, 95%CI 0.30-0.69) for knowing their HIV status, and 68% lower odds (OR=0.32, 95%CI 0.09-0.87) for ever receiving ART. The full table with the adjusted odds ratios for each covariate can be found in the appendix (Table S3.2-4).

3.6 Discussion

Our study confirms the overall hypothesis that the type of multimorbidity is associated with progression in the continuum-of-care. While we confirmed the hypothesis that having concordant diseases is associated with higher likelihood of further care progression, we found the effects of discordant diseases to be mixed, varying across the index diseases examined.

In line with theories and empirical findings from high-income settings described above (12–14), we found that having concordant diseases is associated with higher likelihood of progressing further along the continuum for hypertension and diabetes in our study population. These may be explained by the emphasis that the South African hypertension guidelines place on diabetes and dyslipidemia as important comorbidities, and the emphasis on hypertension and dyslipidemia in the diabetes guidelines (26,27). These guidelines do not give much emphasis to HIV, although both mention it, and neither mention mental disorders. Moreover, providers may be more inclined to urgently treat concordant diseases as a means to reach the target treatment outcomes for the index disease, for example, treating dyslipidemic patients may lead to targeting blood pressure control because of its benefit in preventing the progression of coronary artery diseases (30).

On the other hand, having discordant conditions was not associated with worse care progression for hypertension and diabetes, contrary to what we expected from theory and observations in high-income settings (11,13). Although some studies have shown that mental disorders are associated with poorer care progression for cardiometabolic conditions (30), we did not find a significant effect. Negative findings were observed only among people with HIV, where the presence of discordant cardiometabolic conditions was associated with lower progression in HIV care. This is a concerning finding given that both HIV infection and the use of ART have been associated with increased risk of coronary heart disease and myocardial infarction (31,32). Previous studies that found lower quality of care for non-HIV conditions among HIV patients hypothesized that factors such as lack of specific guidelines for HIV population, under-emphasis on noninfectious chronic disease complications of HIV, prioritization of short term health needs, and the difficulty balancing the demands of caring for complex patients with other medical and psychosocial problems, may have contributed to this finding (17–19).

Comparing across each stage in the continuum-of-care, the presence of concordant and discordant diseases both were associated with higher likelihoods of reaching earlier stages of the continuum for hypertension and diabetes. We posit that this is due to the opportunity costs involved for both providers and patients in being tested or diagnosed, relative to being initiated and adherent to treatment. Testing and diagnosing hypertension involve simple procedures with relatively little effort required from the providers, thus having any type of multimorbidity will likely increase the chance

that the patient will be tested. However, the positive effect of discordant diseases disappears as the opportunity cost increases, as is the case for being initiated for and supported to adhere to treatment, since much more effort is required on the part of the practitioners to determine the right regimen, initiate the treatment, provide counseling for adherence, and follow up regularly to ensure the desired outcomes are met. Measuring blood pressure is a simple procedure, and all patients who walk into the clinic, regardless of their symptoms, are expected to have blood pressure measurements. Thus, having any type of condition, concordant or discordant, will likely increase the chance of the person receiving a blood pressure measurement. For diabetes, those who come in for non-diabetes cardiometabolic conditions may be tested for diabetes given the overlap in the risk factors, pathophysiological pathways, and treatment guidelines. We do not see this positive effect of multimorbidity among people who are HIV infected in our setting, most likely due to reasons such as high levels of stigma, practitioners' lower awareness of HIV among older persons, and that HIV testing requires more sophisticated laboratory testing that takes more effort than, for example, measuring blood pressure. Furthermore, we posit that the negative association between HIV care and having discordant cardiometabolic diseases is in part due to how the clinics in Agincourt sub-district are set up. Those who visit the clinic primarily for HIV testing are directed to a separate nearby building, equipped with health workers tasked solely with testing for HIV. This separate process for HIV testing may explain why those with only HIV and no other discordant diseases were more likely to be diagnosed with HIV conditional on being tested since they likely entered the clinic solely for the purpose of getting HIV care.

The findings also imply that the objective of the South Africa's ICDM model on enhancing the management of co-existing diseases a person may have along with the main disease has not yet been fully met. While not examined empirically in this study, real-life barriers, including long waiting times, staff shortage, and drug stock outs, may have negatively impacted the implementation of ICDM and resulted in less visits made by the patients and short consultation time with the providers. The nurses may not be trained to diagnose or manage all diseases, and given the time constraint they are often only able to address the patient's chief complaint and, in some cases, the concordant diseases that are listed in the guidelines (25). We welcome the introduction of programs such as the Sustainable East Africa Research in Community Health's (SEARCH) campaign and the recently announced U.S. President's Emergency Plan for AIDS Relief (PEPFAR) investment in

implementing joint programs to make cardiometabolic disease management available alongside HIV/AIDS services to bring populations with different types of multimorbidity into care (33–35).

Our study is subject to several limitations. First, we assessed whether the presence of a concordant or discordant condition is associated to the progression in the continuum, not whether being in care for one disease leads to being in care for another. Due to the cross-sectional nature of this study, we cannot determine the temporal sequencing of the diseases nor care progression. We are also unable to assess causality on which type of multimorbidity affects care progression. Second, while the health statuses of the three index diseases and the concordant and discordant diseases were clinically diagnosed, data on the stages to which people progressed were self-reported, and our results may have therefore over or under-reported health seeking behaviors. Third, all conditions within the cardiometabolic and mental diseases were weighted equally, however it is plausible that specific combinations of diseases are associated with higher likelihood of progressing further along the care continuum. Finally, the study's comparability with existing studies and generalizability to low-HIV prevalence settings may be limited.

3.7 Conclusion

To our knowledge, this is one of the first studies to assess the relationship between the multimorbidity type and a patient's progression along the care continuum in LMICs, and the first study to assess its effect on HIV care among people with HIV. We identified how different types of multimorbidity may be affecting at each stage of the continuum-of-care, and concluded that the presence of any type of multimorbidity is associated with higher likelihood of being in stages with lower opportunity costs, while presence of concordant conditions is associated with higher likelihood of being in stages with higher opportunity costs. Our findings from a relatively typical setting in rural South Africa have critical policy implications on enhancing access to testing and treatment services to improve service coverage and population health in South Africa. We could not corroborate causality, but further research to determine this causality – informed by forthcoming waves of the HAALSI study – will improve our understanding of the impact of different the types of multimorbidity on health outcomes and the use of health services. We hope this will prove to be a sound contribution to South African health development.

3.8 References

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3.9 Main Figures and Tables

Table 3.1. Prevalence of concordant and discordant diseases by key sociodemographic covariates among people with hypertension, diabetes, and HIV

Number of people (% among those with the index disease)	**Hypertension**	**Diabetes**	**HIV**
	2,813	512	1,027
Cardiometabolic diseases (excluding index disease)	1535 (55%)	465 (91%)	728 (71%)
Mental disorders	615 (22%)	139 (27%)	181 (18%)
HIV	480 (17%)	77 (15%)	
Age group			
40-49	353 (13%)	45 (9%)	306 (30%)
50-59	757 (27%)	125 (24%)	382 (37%)
60-69	801 (28%)	165 (32%)	237 (23%)
70-79	554 (20%)	116 (23%)	89 (9%)
80+	348 (12%)	61 (12%)	13 (1%)
Sex			
Female	1619 (58%)	298 (58%)	555 (54%)
Male	1194 (42%)	214 (42%)	472 (46%)
Education			
No formal education	1333 (47%)	217 (42%)	419 (41%)
Some primary edu (1-7 y)	987 (35%)	208 (41%)	360 (35%)
Some secondary edu (8-11 y)	294 (10%)	46 (9%)	160 (16%)
Completed secondary (12+ y)	199 (7%)	41 (8%)	88 (9%)
Country of origin			
SA	1998 (71%)	408 (80%)	672 (65%)
Mozambique/Other	815 (29%)	104 (20%)	355 (35%)
Marital status			

Never married	96 (3%)	19 (4%)	75 (7%)
Currently married/living with partner	1457 (52%)	269 (53%)	409 (40%)
Separated/divorced	350 (12%)	54 (11%)	207 (20%)
Widowed	910 (32%)	170 (33%)	336 (33%)
Household size			
Living alone	281 (10%)	49 (10%)	152 (15%)
Living with 1 other person	297 (11%)	57 (11%)	107 (10%)
Living in 3-6 person household	1348 (48%)	245 (48%)	481 (47%)
Living in 7+ person household	887 (32%)	161 (31%)	287 (28%)
Employment status			
Employed (part or full time)	397 (14%)	61 (12%)	220 (21%)
Other	397 (14%)	61 (12%)	220 (21%)
Have limitations in activities of daily living (ADLs)	255 (0%)	68 (0%)	63 (0%)
Wealth index			
Quintile 1 (lowest)	527 (19%)	62 (12%)	253 (25%)
Quintile 2	545 (19%)	84 (16%)	206 (20%)
Quintile 3	542 (19%)	105 (21%)	213 (21%)
Quintile 4	600 (21%)	121 (24%)	195 (19%)
Quintile 5 (highest)	599 (21%)	140 (27%)	160 (16%)

Table 3.2. Association between the progression in the continuum-of-care and concordant/discordant disease status and key sociodemographic covariates among people with hypertension, diabetes, and HIV

	Dependent variable: progression in care continuum (number of steps)		
	Hypertension	Diabetes	HIV
	(1)	(2)	(3)
Observations	2,813	512	1,027
Cardiometabolic (without index)	0.33*** (0.23, 0.44)	1.30***(0.79, 1.82)	-0.33**(-0.54, -0.11)
Mental	0.25*** (0.12, 0.38)	0.06 (-0.28, 0.40)	0.001 (-0.25, 0.25)
HIV	0.19* (0.04, 0.33)	0.15 (-0.27, 0.57)	
Age group (ref: 40-49)			
50-59	0.28** (0.09, 0.47)	0.46 (-0.14, 1.06)	0.33* (0.08, 0.58)
60-69	0.52*** (0.32, 0.72)	0.41 (-0.20, 1.02)	0.22 (-0.09, 0.53)
70-79	0.76*** (0.54, 0.99)	0.52 (-0.15, 1.18)	0.10 (-0.31, 0.51)
80+	0.64*** (0.38, 0.89)	0.39 (-0.37, 1.14)	-0.19 (-1.08, 0.69)
Sex: female	0.54*** (0.42, 0.66)	-0.02 (-0.36, 0.32)	-0.24* (-0.45, -0.03)
Education (ref: no formal edu)			
Some primary (1-7 yrs)	-0.02 (-0.15, 0.11)	0.03 (-0.32, 0.38)	0.16 (-0.09, 0.41)
Some secondary (8-11 yrs)	-0.16 (-0.37, 0.04)	0.23 (-0.38, 0.84)	0.08 (-0.27, 0.43)
Secondary or more (12+ yrs)	-0.29* (-0.55, -0.03)	0.43 (-0.24, 1.10)	-0.02 (-0.45, 0.41)
Country of origin (ref: South Africa)			
Mozambique/others	-0.19** (-0.32, -0.05)	-0.10 (-0.49, 0.30)	-0.02 (-0.25, 0.21)
Household size (ref: living alone)			
Living with another person	0.11 (-0.13, 0.35)	-0.02 (-0.68, 0.63)	0.21 (-0.18, 0.60)
Living with 3-6 persons	0.02 (-0.18, 0.21)	-0.10 (-0.65, 0.44)	0.39* (0.08, 0.70)
Living with 7+ persons	0.06 (-0.15, 0.27)	-0.02 (-0.60, 0.55)	0.13 (-0.21, 0.46)
Marital status (ref: Currently married or living with partner)			
Never married	-0.08 (-0.39, 0.22)	-0.10 (-0.93, 0.72)	-0.15 (-0.55, 0.25)
Separated/Divorced	-0.14 (-0.33, 0.04)	-0.18 (-0.71, 0.35)	0.16 (-0.12, 0.44)
Widowed	-0.10 (-0.25, 0.04)	0.05 (-0.34, 0.43)	0.10 (-0.15, 0.34)
Employed (part/full time)	-0.10 (-0.27, 0.06)	-0.04 (-0.53, 0.45)	-0.11 (-0.35, 0.14)
Have limitations in activities of daily living (ADLs)	0.34*** (0.15, 0.53)	0.47*(0.03, 0.92)	0.33(-0.08, 0.73)
Wealth quintile (ref: quintile 1)			
Quintile 2	0.07 (-0.10, 0.24)	-0.12 (-0.67, 0.43)	0.15 (-0.14, 0.44)
Quintile 3	0.17 (-0.01, 0.35)	-0.04 (-0.57, 0.49)	0.04 (-0.25, 0.34)
Quintile 4	0.21* (0.03, 0.38)	-0.06 (-0.59, 0.46)	0.22 (-0.09, 0.53)
Quintile 5	0.45*** (0.26, 0.64)	0.07 (-0.49, 0.63)	0.32 (-0.03, 0.67)
Constant	1.30*** (0.98, 1.62)	0.62 (-0.37, 1.61)	2.67*** (2.19, 3.15)

*p<0.05; **p<0.01; ***p<0.001

Green: concordant diseases

Orange: discordant diseases

Table 3.3. Factors associated with the progression to each stage in the continuum-of-care for hypertension, diabetes, and HIV

		Tested (all pop)	Tested (among those with disease)	Know status (among tested)	Ever treated (among those who know status)	Currently treated (among ever treated)
		(1)	(2)	(3)	(4)	(5)
Hypertension	Observations	4,447	2,813	2,084	1,915	1,508
	Concordant: Cardiometabolic	1.13	1.17	1.53***	1.52***	1.46*
		(0.99, 1.29)	(0.98, 1.39)	(1.24, 1.88)	(1.21, 1.92)	(1.08, 1.97)
	Discordant: Mental	1.32**	1.44**	1.52**	1.22	1.04
		(1.11, 1.57)	(1.15, 1.82)	(1.17, 1.99)	(0.91, 1.64)	(0.74, 1.50)
	Discordant: HIV	1.20*	1.29*	1.31	0.85	1.26
		(1.02, 1.42)	(1.01, 1.65)	(0.99, 1.74)	(0.63, 1.14)	(0.83, 1.95)
Diabetes	Observations	4,447	512	383	300	252
	Concordant: Cardiometabolic	1.75***	4.20***	3.55*	3.03	2.88
		(1.51, 2.04)	(2.19, 8.19)	(1.34, 9.64)	(0.67, 12.21)	(0.27, 22.57)
	Discordant: Mental	1.13	1.36	0.76	0.72	1.68
		(0.97, 1.31)	(0.82, 2.31)	(0.44, 1.33)	(0.35, 1.55)	(0.57, 5.50)
	Discordant: HIV	1.10	1.07	1.29	0.81	0.43
		(0.94, 1.28)	(0.60, 1.98)	(0.62, 2.87)	(0.32, 2.18)	(0.14, 1.40)
HIV	Observations	4,447	1,027	913	730	703
	Discordant: Cardiometabolic	1.06	1.03	0.46***	0.32*	0.00
		(0.90, 1.25)	(0.66, 1.58)	(0.30, 0.69)	(0.09, 0.87)	(-Inf, Inf)
	Discordant: Mental	0.99	1.03	0.98	1.20	0.57
		(0.85, 1.17)	(0.61, 1.83)	(0.64, 1.53)	(0.41, 4.44)	(0.06, 12.26)

*p<0.05; **p<0.01; ***p<0.001

Green: concordant diseases

Orange: discordant diseases

3.10 Supplemental Material

S3.1. Disease status of concordant and discordant diseases

In addition to the three index diseases (hypertension, diabetes, HIV), we selected five concordant and discordant diseases for the study. Below we describe the definitions of each:

Dyslipidemia. Considered with the disease if met one of the following criteria: self-reported disease status, elevated total cholesterol (≥6.21 mmol/L), low HDL (1.19 mmol/L), elevated LDL (>4.1 mmol/L), elevated triglycerides (>2.25 mmol/L).

Angina was diagnosed using the Rose Chest Pain Questionnaire (1).

Depression: symptoms of depression were screened using the Center for Epidemiological Studies Depression Scale 8-item questionnaire, setting the cutoff at three or more symptoms (2).

Post-traumatic stress disorder (PTSD) was diagnosed if four or more symptoms on a seven-symptom screening scale were present (3).

Alcohol dependence was defined using the CAGE questionnaire (4).

S3.2. Full results table of factors associated with the progression to each stage in the continuum-of-care for hypertension

Table S3.1. Factors associated with the progression to each stage in the continuum-of-care for hypertension (expressed as odds ratios)

	Dependent variable:				
	Tested (all pop)	Tested (among HTN+)	Diagnosed	Ever treated	Currently treated
Observations	4,447	2,813	2,084	1,915	1,508
Concordant: Cardiometabolic (without HTN)	1.13	1.17	1.53***	1.52***	1.46*
	(0.99, 1.29)	(0.98, 1.39)	(1.24, 1.88)	(1.21, 1.92)	(1.08, 1.97)
Discordant: Mental	1.32**	1.44**	1.52**	1.22	1.04
	(1.11, 1.57)	(1.15, 1.82)	(1.17, 1.99)	(0.91, 1.64)	(0.74, 1.50)
Discordant: HIV	1.20*	1.29*	1.31	0.85	1.26
	(1.02, 1.42)	(1.01, 1.65)	(0.99, 1.74)	(0.63, 1.14)	(0.83, 1.95)
Age group (ref: 40-49)					
50-59	1.16	1.27	1.18	1.87***	0.99
	(0.95, 1.42)	(0.95, 1.71)	(0.83, 1.67)	(1.29, 2.69)	(0.56, 1.70)
60-69	1.31*	1.49*	1.48*	2.76***	1.71
	(1.05, 1.64)	(1.08, 2.05)	(1.01, 2.16)	(1.83, 4.17)	(0.92, 3.12)
70-79	1.55***	1.68**	2.28***	2.96***	1.61
	(1.19, 2.01)	(1.17, 2.40)	(1.48, 3.52)	(1.88, 4.68)	(0.84, 3.05)
80+	1.55**	1.41	1.72*	3.18***	1.56
	(1.13, 2.13)	(0.94, 2.13)	(1.06, 2.81)	(1.84, 5.55)	(0.76, 3.21)
Sex: female	1.40***	1.73***	1.94***	1.61***	1.08
	(1.21, 1.63)	(1.42, 2.12)	(1.53, 2.46)	(1.23, 2.11)	(0.75, 1.55)
Education (ref: no formal edu)					
Some primary	1.01	1.03	0.99	0.64**	0.79
	(0.85, 1.19)	(0.83, 1.28)	(0.77, 1.29)	(0.48, 0.86)	(0.55, 1.14)
Some secondary	1.13	0.99	0.70	0.66	1.08
	(0.88, 1.45)	(0.72, 1.39)	(0.48, 1.03)	(0.43, 1.03)	(0.58, 2.10)
Secondary or more	0.72*	0.85	0.80	0.46**	0.72
	(0.54, 0.97)	(0.57, 1.28)	(0.49, 1.32)	(0.27, 0.79)	(0.34, 1.58)
Country of origin (ref: South Africa)					
Mozambique/others	1.01	0.91	0.69**	0.76	0.78
	(0.86, 1.19)	(0.73, 1.13)	(0.54, 0.89)	(0.57, 1.02)	(0.54, 1.12)
Household size (ref: living alone)					
Living with another person	1.22	1.38	0.79	1.04	0.87
	(0.90, 1.65)	(0.93, 2.06)	(0.49, 1.25)	(0.59, 1.81)	(0.45, 1.68)
Living with 3-6 persons	1.01	1.02	0.98	0.82	1.00
	(0.79, 1.28)	(0.74, 1.40)	(0.66, 1.46)	(0.52, 1.29)	(0.57, 1.72)
Living with 7+ persons	1.01	1.30	0.96	0.81	1.03
	(0.78, 1.30)	(0.93, 1.82)	(0.63, 1.45)	(0.49, 1.29)	(0.57, 1.83)
Marital status (ref: Currently married or living with partner)					
Never married	0.89	0.84	1.04	0.54*	1.38
	(0.66, 1.22)	(0.53, 1.37)	(0.58, 1.93)	(0.30, 0.97)	(0.55, 4.21)
Separated /divorced	0.94	0.76	0.90	1.08	0.90

	(0.75, 1.18)	(0.56, 1.02)	(0.63, 1.30)	(0.71, 1.65)	(0.55, 1.51)
Widowed	0.91	0.85	0.94	0.82	1.14
	(0.76, 1.09)	(0.66, 1.08)	(0.71, 1.25)	(0.60, 1.12)	(0.76, 1.69)
Employed (part/full time)	1.06	1.02	0.66**	0.80	1.04
	(0.87, 1.28)	(0.79, 1.33)	(0.49, 0.90)	(0.57, 1.12)	(0.64, 1.75)
Have limitations in activities of daily living (ADLs)					
	2.85***	3.36***	1.09	1.59	0.79
	(2.08, 4.00)	(2.21, 5.33)	(0.77, 1.57)	(1.01, 2.60)	(0.50, 1.28)
Wealth quintile (ref: quintile 1)					
Quintile 2	1.10	1.11	0.87	1.27	1.13
	(0.90, 1.34)	(0.84, 1.47)	(0.63, 1.21)	(0.86, 1.88)	(0.72, 1.78)
Quintile 3	1.40**	1.21	1.05	0.79	1.72*
	(1.13, 1.73)	(0.91, 1.61)	(0.75, 1.48)	(0.54, 1.15)	(1.04, 2.87)
Quintile 4	1.26*	1.02	1.08	1.20	1.44
	(1.02, 1.56)	(0.77, 1.36)	(0.76, 1.52)	(0.81, 1.76)	(0.90, 2.33)
Quintile 5	1.55***	1.38*	1.65**	1.58*	1.73*
	(1.23, 1.96)	(1.02, 1.88)	(1.13, 2.39)	(1.04, 2.39)	(1.04, 2.91)
Constant	1.03	1.03	1.18	1.56	2.76*
	(0.71, 1.47)	(0.62, 1.71)	(0.64, 2.19)	(0.78, 3.15)	(1.12, 6.99)

*p<0.05; **p<0.01; ***p<0.001

S3.3. Full results table of factors associated with the progression to each stage in the continuum-of-care for diabetes

Table S3.2. Factors associated with the progression to each stage in the continuum-of-care for diabetes (expressed as odds ratios)

	Dependent variable:				
	Tested (all pop)	Tested (among DM+)	Diagnosed	Ever treated	Currently treated
Observations	4,447	512	383	300	252
Concordant: Cardiometabolic (without DM)	1.75***	4.20***	3.55*	3.03	2.88
	(1.51, 2.04)	(2.19, 8.19)	(1.34, 9.64)	(0.67, 12.21)	(0.27, 22.57)
Discordant: Mental	1.13	1.36	0.76	0.72	1.68
	(0.97, 1.31)	(0.82, 2.31)	(0.44, 1.33)	(0.35, 1.55)	(0.57, 5.50)
Discordant: HIV	1.10	1.07	1.29	0.81	0.43
	(0.94, 1.28)	(0.60, 1.98)	(0.62, 2.87)	(0.32, 2.18)	(0.14, 1.40)
Age group (ref: 40-49)					
50-59	1.09	1.11	2.12	3.63	0.65
	(0.90, 1.32)	(0.48, 2.53)	(0.75, 5.91)	(0.73, 17.01)	(0.03, 5.72)
60-69	1.33**	1.24	2.15	0.79	0.74
	(1.08, 1.65)	(0.53, 2.85)	(0.77, 5.90)	(0.17, 3.12)	(0.03, 7.66)
70-79	1.45**	2.10	1.64	1.93	0.19
	(1.14, 1.85)	(0.81, 5.37)	(0.54, 4.90)	(0.35, 9.67)	(0.01, 1.80)
80+	1.44*	1.47	1.46	1.57	0.15
	(1.08, 1.92)	(0.50, 4.34)	(0.42, 5.12)	(0.25, 9.62)	(0.01, 1.65)
Sex: female	1.29***	1.10	0.74	1.03	1.82
	(1.13, 1.49)	(0.67, 1.80)	(0.41, 1.34)	(0.45, 2.35)	(0.60, 5.81)
Education (ref: no formal edu)					
Some primary	1.22**	1.06	0.99	1.16	2.31
	(1.05, 1.42)	(0.63, 1.77)	(0.55, 1.77)	(0.51, 2.65)	(0.82, 6.88)
Some secondary	1.38**	1.33	1.66	0.84	0.83
	(1.10, 1.75)	(0.56, 3.31)	(0.57, 5.31)	(0.23, 3.42)	(0.15, 5.12)
Secondary or more	1.10	1.54	2.43	0.90	1.21
	(0.83, 1.46)	(0.58, 4.42)	(0.68, 10.40)	(0.21, 4.18)	(0.20, 8.46)
Country of origin (ref: South Africa)					
Mozambique/others	0.93	0.96	1.03	0.83	0.43
	(0.80, 1.08)	(0.54, 1.72)	(0.55, 1.98)	(0.34, 2.11)	(0.16, 1.21)
Household size (ref: living alone)					
Living with another person	1.15	0.95	0.67	1.54	7.22
	(0.87, 1.51)	(0.34, 2.61)	(0.22, 1.96)	(0.38, 6.29)	(0.83, 159.87)
Living with 3-6 persons	1.14	0.76	0.71	1.67	1.12
	(0.91, 1.43)	(0.33, 1.67)	(0.27, 1.71)	(0.49, 5.15)	(0.24, 4.39)
Living with 7+ persons	1.11	0.82	1.11	1.62	1.03
	(0.87, 1.41)	(0.34, 1.89)	(0.40, 2.88)	(0.47, 5.18)	(0.21, 4.33)
Marital status (ref: Currently married or living with partner)					
Never married	0.63**	0.70	1.92	2.55	0.39
	(0.46, 0.85)	(0.24, 2.18)	(0.45, 10.41)	(0.27, 67.18)	(0.03, 10.56)
Separated /divorced	1.05	0.96	1.14	0.60	0.26
	(0.85, 1.29)	(0.45, 2.13)	(0.48, 2.79)	(0.19, 2.08)	(0.05, 1.29)

Widowed	0.89	0.99	1.43	0.90	0.40
	(0.76, 1.05)	(0.56, 1.73)	(0.74, 2.80)	(0.36, 2.25)	(0.11, 1.40)
Employed (part/full time)	1.14	1.38	0.90	0.53	0.43
	(0.95, 1.37)	(0.69, 2.91)	(0.38, 2.25)	(0.18, 1.66)	(0.09, 2.10)
Have limitations in activities of daily living (ADLs)					
	1.81***	1.78	2.24*	0.85	0.54
	(1.43, 2.29)	(0.88, 3.87)	(1.06, 5.15)	(0.34, 2.29)	(0.18, 1.64)
Wealth quintile (ref: quintile 1)					
Quintile 2	1.00	0.69	1.41	1.53	0.72
	(0.83, 1.22)	(0.32, 1.49)	(0.55, 3.59)	(0.33, 7.35)	(0.09, 4.44)
Quintile 3	1.21	1.02	1.04	0.82	0.80
	(0.99, 1.47)	(0.47, 2.17)	(0.44, 2.43)	(0.20, 3.00)	(0.09, 4.96)
Quintile 4	1.36**	1.13	1.27	0.68	0.25
	(1.12, 1.66)	(0.52, 2.41)	(0.53, 2.98)	(0.17, 2.40)	(0.03, 1.29)
Quintile 5	1.53***	0.99	1.74	0.64	0.27
	(1.24, 1.89)	(0.44, 2.17)	(0.68, 4.46)	(0.16, 2.35)	(0.03, 1.58)
Constant	0.27***	0.59	0.42	1.44	18.26
	(0.19, 0.38)	(0.15, 2.36)	(0.07, 2.43)	(0.13, 18.14)	(0.58, 1,275)

*p<0.05; **p<0.01; ***p<0.001

S3.4. Full results table of factors associated with the progression to each stage in the continuum-of-care for HIV

Table S3.3. Factors associated with the progression to each stage in the continuum-of-care for HIV (expressed as odds ratios)

	Dependent variable:				
	Tested (all pop)	Tested (among HIV+)	Know status	Ever treated	Currently treated
Observations	4,447	1,027	913	730	703
Discordant: Cardiometabolic	1.06	1.03	0.46***	0.32*	0.00
	(0.90, 1.25)	(0.66, 1.58)	(0.30, 0.69)	(0.09, 0.87)	(-Inf, Inf)
Discordant: Mental	0.99	1.03	0.98	1.20	0.57
	(0.85, 1.17)	(0.61, 1.83)	(0.64, 1.53)	(0.41, 4.44)	(0.06, 12.26)
Age group (ref: 40-49)					
50-59	1.06	1.99*	1.13	2.81*	0.71
	(0.85, 1.31)	(1.17, 3.44)	(0.74, 1.74)	(1.09, 7.77)	(0.03, 9.81)
60+	0.59***	1.25	1.04	6.53*	1.58
	(0.48, 0.73)	(0.71, 2.19)	(0.63, 1.71)	(1.71, 33.09)	(0.05, 51.26)
Sex: female	1.22**	0.73	0.79	0.40	1.64
	(1.05, 1.40)	(0.47, 1.14)	(0.55, 1.15)	(0.14, 1.04)	(0.07, 15.93)
Education (ref: no formal edu)					
Some primary	1.64***	1.74*	0.89	1.61	0.62
	(1.41, 1.93)	(1.03, 2.97)	(0.57, 1.38)	(0.49, 5.44)	(0.04, 6.97)
Above primary	1.85***	1.80	0.73	0.94	Inf
	(1.47, 2.33)	(0.91, 3.59)	(0.41, 1.29)	(0.23, 3.65)	(0.00, Inf)
Country of origin: Mozambique/other	1.17	1.08	0.83	1.62	0.79
	(1.00, 1.37)	(0.67, 1.73)	(0.55, 1.26)	(0.56, 4.97)	(0.07, 8.58)
Household size: not living alone	0.98	1.31	1.70*	0.42	0.00
	(0.78, 1.22)	(0.71, 2.30)	(1.04, 2.72)	(0.02, 2.28)	(-Inf, Inf)
Marital status: Not currently married or living with partner	0.89	1.24	1.01	1.59	0.00
	(0.77, 1.03)	(0.79, 1.95)	(0.69, 1.49)	(0.64, 3.92)	(-Inf, Inf)
Employed: part/full time	1.28*	0.87	0.82	1.34	Inf
	(1.04, 1.58)	(0.53, 1.47)	(0.54, 1.24)	(0.52, 3.98)	(0.00, Inf)
Have limitations in activities of daily living (ADLs)					
	1.07	4.35*	1.04	0.47	Inf
	(0.85, 1.36)	(1.31, 26.96)	(0.54, 2.13)	(0.11, 3.29)	(0.00, Inf)
Wealth quintile (ref: quintile 1)					
Quintile 2	1.12	1.43	0.93	3.26	1.60
	(0.92, 1.36)	(0.79, 2.63)	(0.56, 1.53)	(0.88, 15.75)	(0.12, 41.44)
Quintile 3	1.24*	1.14	0.88	1.98	Inf
	(1.01, 1.52)	(0.64, 2.06)	(0.53, 1.48)	(0.57, 7.59)	(0.00, Inf)
Quintile 4 & 5	1.40***	1.56	1.17	1.92	2.47
	(1.16, 1.69)	(0.87, 2.80)	(0.70, 1.95)	(0.60, 6.20)	(0.16, 71.67)
Constant	1.45*	2.66*	6.05***	37.85**	Inf
	(1.02, 2.06)	(1.07, 6.85)	(2.61, 14.43)	(3.78, 966.39)	(0.00, Inf)

*p<0.05; **p<0.01; ***p<0.001

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Chapter 4. Estimating the distribution of morbidity and mortality of childhood diarrhea, measles, and pneumonia by socio-economic group in low- and middle-income countries

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4.1 Abstract

Background

Various social policies have been directed toward enhancing equity through health policies, but disaggregated data on health outcomes by population subgroups are often unavailable, and methods for estimating health benefits gained across different subgroups are lacking. This chapter develops a model to estimate the distribution of childhood disease cases and deaths across income groups, and the benefits of three vaccine programs in 41 low- and middle-income countries.

Methods

For each country and for three diseases (diarrhea, measles, pneumonia), we estimated the distributions of cases and deaths that would occur across income quintiles in the absence of any immunization or treatment programs, using both the prevalence and relative risk of a set of risk and prognostic factors. Building on these baseline estimates, we examined the impact of three vaccines (first dose of measles vaccine, pneumococcal conjugate vaccine, and rotavirus vaccine), under five scenarios based on different sets of quintile-specific immunization coverage and disease treatment utilization rates.

Results

Due to higher prevalence of risk factors among the poor, more disease cases and deaths would occur among the poorest two quintiles for all three diseases when vaccines or treatment are unavailable. Compared to this null counterfactual scenario, we find that current immunization coverage and treatment utilization rates have resulted in increased inequity in the distribution of cases and deaths. Country-specific context, including how the baseline risks, immunization coverage, and treatment utilization are currently distributed across quintiles, affects how different policies translate into changes in cases and deaths distribution.

Conclusions

Our study highlights several factors that would substantially contribute to the unequal distribution of childhood diseases, and find that merely ensuring equal access to vaccines will not reduce the health

outcomes gap across income quintiles. Such information can inform policies and planning of programs that aim to improve equitable delivery of healthcare services.

Funding

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4.2 Keywords

Diarrhea, measles, pneumonia, vaccines, risk factors, equity.

4.3 Introduction

With the ambitious goals of ending extreme poverty and fighting against inequity in low- and middle-income countries (LMICs) (1), international agencies such as the World Bank have advocated for improving access to essential services, such as health care and education, for the lowest 40% of income earners (2). Policymakers in LMICs, where often vast inequities in health exist, are interested in enhancing equity for both ethical and political reasons (3,4).

Vaccine programs have been recognized as one of the most successful interventions in improving population health worldwide. Efforts put forward by local governments and international agencies have contributed to raising childhood vaccine coverage in the last decade (5), though high child mortality is still observed in LMICs, with about 5.9 million under-five deaths in 2015 (6). More recently, the Global Vaccine Action Plan and Gavi the Vaccine Alliance both listed equitable access to vaccination as their top priorities (11–13). However, it is unclear whether ensuring equitable access to vaccines leads to health equity, which we define as equality of health outcomes across population subgroups. To answer this question, one needs to compare how disease burden was distributed across before and after the introduction of vaccines by subgroups. However, such data on disease burden by socioeconomic strata before and after vaccines are not available empirically, making it difficult to design equitable policies for populations. The objective of this work is therefore to introduce an analytical approach to estimate the distribution of childhood disease cases and deaths and the benefits of three vaccine programs by socioeconomic group.

4.4 Methods

We examined three major childhood diseases: measles, pneumonia, and diarrhea. These diseases were selected as they represent 23% of deaths (1%, 13%, and 9%, respectively) occurring among under-five children in LMICs (6). We studied the three corresponding vaccines: measles vaccine (routine first dose, MCV1), rotavirus vaccine (RV, against rotavirus diarrhea), and pneumococcal conjugate vaccine (PCV, against pneumococcal pneumonia).

The approach is based on the concept of population attributable fraction (PAF) (14). Using PAF, we quantified the contribution of sets of risk and prognostic factors, defined as behaviors and

characteristics of an individual that can be used to estimate the likelihood of contracting and dying from each disease. The proportion of cases and deaths that can be attributed to the exposure of selected sets of risk and prognostic factors are classified as attributable, and the remaining as unattributable cases and deaths. Our model takes advantage of the differences in the prevalence of risk and prognostic factors across socioeconomic strata to estimate the distribution of cases and deaths. A flow diagram outlining each step is presented in Figure 4.1.

Analytical structure

Cases. For each risk factor, we defined w_j as the relative weight assigned to risk factor j, and RR_j as the relative risk of risk factor j: $w_j = \frac{RR_j}{\sum_{k=1}^{n} RR_k}$. Subsequently, the proportion of attributable cases (Ac_i) occurring in income quintile i, can be estimated as:

$$Ac_i = \frac{\sum_{j=1}^{n} w_j P_{ij}}{\sum_{k=1}^{5} \sum_{j=1}^{n} w_j P_{kj}}, \quad (1)$$

where P_{ij} is the prevalence of risk factor j in income quintile i (Step 1 in Figure 4.1).

In the presence of a vaccine program, we added quintile-specific vaccine coverage (V_i) and vaccine efficacy (E, assumed constant for simplicity) to estimate the cases not averted by the program (Step 2 in Figure 4.1):

$$Ac_{v,i} = \frac{(1-V_i E) \sum_{j=1}^{n} w_j P_{ij}}{\sum_{k=1}^{5} [(1-V_k E) \sum_{j=1}^{n} w_j P_{kj}]}, \quad (2)$$

Deaths. Whether a case results in death depends not only on the prevalence and relative risk of each prognostic factor, which impacts the case fatality ratio (CFR) observed in each quintile, but also on individuals' care seeking behavior. Similar to the step above, we first assigned weights to each

prognostic factor contributing to disease mortality: $u_l = \frac{RR_l}{\sum_{k=1}^{m} RR_k}$, where u_l is the relative weight assigned to prognostic factor l, and RR_l is the relative risk of prognostic factor l. The weight and the prevalence of the prognostic factor determine CFR for each quintile. We applied country-specific CFR calculated from the Global Burden of Disease (GBD) study database (incidence divided by mortality) as the average CFR across all quintiles (CFR_{avg}) (15), and estimated the CFR per income quintile i as: $CFR_i = \frac{\sum_{l=1}^{m} u_l P_{il}}{\sum_{l=1}^{m} u_l P_{avg,l}} \times CFR_{avg}$, where P_{il} is the prevalence of prognostic factor l in quintile i and $P_{avg,l}$ is the average prevalence across quintiles. Hence, the proportions of attributable (Ad_i) deaths occurring in quintile i become:

$$Ad_i = \frac{CFR_i(1-a_i Eff)}{\sum_{k=1}^{5} CFR_k(1-a_k Eff)}, \quad (3)$$

where a_i is the proportion of cases in quintile i for whom treatment was sought from a health facility, and Eff is the effectiveness of the care provided (assumed constant) (Step 3 in Figure 4.1).

For the unattributable portion, we assumed that the cases and deaths were distributed equally across quintiles.

$$UAc_{v,i} = \frac{(1-V_i E)}{\sum_{k=1}^{5}(1-V_k E)}. \quad (4)$$

$$UAd_i = \frac{(1-a_i Eff)}{\sum_{k=1}^{5}(1-a_k Eff)}. \quad (5)$$

Thus, formally, for each disease:

$$C_i = Ac_i \times TC_a + UAc_i \times TC_{ua}, \quad (6)$$

$$D_i = Ad_i \times TD_a + UAd_i \times TD_{ua} , \quad (7)$$

where C_i and D_i are the numbers of cases and deaths in income quintile i, TC_a and TC_{ua} are the total cases attributable and unattributable to risk factors, and TD_a and TD_{ua} are the total deaths attributable and unattributable to prognostic factors.

A summary of all the symbols used and corresponding parameters is summarized in Table 4.1.

Data sources

LMICs with Demographic and Health Surveys (DHS) available after 2010 were selected (the full list is in Appendix S4.1). We first searched the literature for risk and prognostic factors with the highest relative risks for diarrhea, measles, and pneumonia. For each factor, we also checked its availability by quintile-specific prevalence rate in the DHS (16). Factors that did not match with DHS variables, had poor data quality, or poor variable definition were excluded (listed in Table 4.2). We shortlisted four to five factors per disease (Table 4.2, for more details see Appendix S4.2). From the DHS, we used the percentage of those seeking care from a health provider for different conditions: the percentage who sought care among those with acute respiratory infection (ARI, for pneumonia) and diarrhea, respectively; for measles, the average of the proportions among those with ARI and diarrhea.

We collected country-specific data on the proportion of disease-specific cases and deaths that can be attributable to sets of risk and prognostic factors. The average percentage of attributable cases (deaths) in the selected countries were 73% (76%) for measles, 92% (94%) for pneumonia, and 95% (97%) for diarrhea (17). In other words, under-five cases and deaths for those diseases were largely attributable to the selected risk and prognostic factors.

Outcomes and scenarios

Per disease, we first estimated the distribution of cases across quintiles without immunization. Second, we assessed the impact of vaccine programs (MCV1, PCV, RV) on this distribution. Third, we estimated the change in the distribution of deaths among cases not averted by vaccines under different treatment utilization scenarios.

For both cases and deaths, we selected five scenarios. For cases, Scenario 1 (S1) assumes zero vaccine coverage, which captures today's status in many LMICs for PCV and RV (not MCV1). S2 incorporates differences in current vaccine coverage across quintiles. We used vaccine coverage estimates from Gavi for 2016 (18). To obtain quintile-specific MCV1 coverage, we multiplied these estimates with the quintile-specific MCV1 coverage rates obtained from the DHS. For PCV and RV, for which the DHS did not have coverage information, we multiplied the national average with the DHS ratios of three- and two-dose quintile-specific diphtheria-tetanus-pertussis vaccine (DPT) coverage rates, since PCV and RV match DPT's three- and two-dose schedules, respectively. We assumed these vaccines only benefitted children who received all the recommended doses (three for PCV and two for RV), and not among those who were partially vaccinated, even though partial vaccination may provide some degree of protection. To examine the effect of redistributing existing doses on health equity, S3 maintains the same total number of vaccines available in each country as S2, but distributes equal number of doses to each quintile. In other words, S3 measures how much equity gain a country would see purely through redistribution without purchasing any additional vaccines. S4 assumes that vaccine coverage per quintile is proportional to the morbidity risk assigned to that quintile. In other words, those with a higher risk of getting the disease have a higher probability of receiving the vaccine. S5 first reduces the baseline morbidity risks of all quintiles to the lowest risk level observed in the country (i.e., lowest prevalence of each risk factor), such that all quintiles have the same number of cases, and then applies the most recent Gavi-projected quintile-specific vaccine coverage.

For deaths among cases that were not averted by vaccine programs, S1 examines the distribution of deaths under the hypothetical scenario of people not utilizing treatment. S2 reflects the differences in the current treatment utilization rates across income quintiles and how these lead to unequal

distribution of remaining deaths. S3 assumes equal utilization (at the national average) across all quintiles. S4 assumes that quintile-specific utilization is proportional to quintile-specific CFR, i.e., those with a higher risk of dying from the disease have a higher probability of utilization. Finally, S5 assumes that CFR is set at the lowest level observed in the country for all quintiles and applied most recent DHS-reported quintile-specific utilization rates.

For each scenario, we calculated: (i) the number of cases and deaths by quintile, and (ii) the change in the distribution of remaining cases and deaths. For (i), we assumed a starting point of 100% of cases or deaths when no vaccine programs are present and calculated the reduction in the total burden under each scenario. For (ii), we explored the area under the curve (AUC) of the cumulative percentage of cases (or deaths) by quintile, and calculated the changes in the AUC per scenario. For example, an increase in the AUC after vaccine program suggests that, among the remaining cases not averted by the program, a higher percentage of cases would be among the poorer quintiles compared to prior vaccine introduction.

Sensitivity analysis

Three sets of sensitivity analyses were conducted. First, we accounted for the differences in the sizes of the under-five population in each quintile by adjusting the number of cases and deaths with the quintile-specific total fertility rate. Second, instead of assuming that unattributable cases and deaths ($\mathrm{UAc_i}$ and $\mathrm{UAd_i}$) were distributed equally across quintiles, we used the ratios of quintile-specific under-five mortality rates ($\mathrm{U5M}_i$) to the national average for adjustment. Third, to account for the uncertainty in the estimates of relative risks, we conducted one-way sensitivity analyses for each risk and prognostic factor. The results are presented in Appendix S4.4.

4.5 Results

Results for all countries are available in Appendix S4.3. To illustrate, we display our findings for each disease for three populous country examples: Nigeria, Pakistan, and Ethiopia.

Measles

Under the hypothetical scenario of no vaccine (S1), more measles cases would occur among the poorer quintiles. In Nigeria, Pakistan, and Ethiopia, the two bottom quintiles would account for 49, 51, and 48% of all cases, in comparison to 31, 31, and 32% in the top two quintiles (S1, Figure 4.2). With MCV1 (S2), where coverage is higher among the richer quintiles, a higher proportion of cases would be averted in the top two quintiles. Compared to S1, AUC would increase by 21, 16, and 13% in each country, suggesting that the distribution of remaining measles cases is further skewed towards the poor with MCV1.

S3 assumes equal number of MCV1 across quintiles, hence the same number of cases would be averted per quintile, leading to larger AUC than S1 (since the poor would still have more remaining cases because of the unequal distribution of baseline morbidity risk ex-ante), but smaller AUC than S2 (more equal distribution of the vaccine). Distributing vaccines proportionally to quintile-specific risks (S4) would substantially reduce the unequal distribution. In S5, we estimated a larger proportion of cases being averted (compared to S2 and S3), suggesting that addressing the underlying morbidity is an effective strategy to reduce overall burden. The increase in AUC is mainly due to the unequal distribution of vaccine coverage. The magnitude of increase in AUC differs by country: for example, Nigeria and Ethiopia have larger gaps in vaccine coverage between rich and poor, leading to larger increases in AUC.

Each quintile faces different disease-specific mortality rates due to differences in the CFR and the probability of seeking treatment. When treatment is not available, deaths among measles cases not averted by MCV1 are heavily concentrated in the poorest quintile: 42, 53, and 34% in each country, respectively (S1). Even when seeking treatment under current quintile-specific utilization rates, these unequal distributions remain because the proportion of seeking treatment is much lower among the poor (S2). S3 assumes equal treatment utilization per quintile, resulting in a higher number of deaths averted by treatment and no distribution change (from S1) from the unequal distribution of the underlying mortality risks. If treatment utilization patterns were proportional to CFR, substantial increases in the percentage of deaths averted by treatment and decreases in AUC in each country would be seen (S4). If instead the unequal distribution of prognostic factors was flattened and

current quintile-specific treatment utilization was maintained, a 1% increase in the total number of cases averted by treatment would be seen in each country but with larger decreases in AUC, especially in Nigeria and Pakistan where the initial death distributions were more skewed toward the poor (S5).

Pneumonia

Pneumonia cases are estimated to be concentrated among the poor (S1) (Figure 4.3). For Nigeria, the assumed difference in PCV coverage across quintiles is large; thus a larger proportion of pneumonia cases would be averted among the top two quintiles, resulting in increases in AUC (S2). Even after equalizing dosage distribution, minimal changes would occur in both the number of cases averted and the relative distribution of the remaining cases (S3). Distributing PCV in proportion to baseline risks would lead to increases in the cases averted and reductions in AUC (S4). Instead, equalizing baseline risks first and then applying current coverage rates would lead to small improvements in both the number of averted cases and AUC in Nigeria and Ethiopia, but larger effects on AUC in Pakistan because of a more skewed distribution towards the poor at baseline.

Under S1, the poorest quintile would have experienced 32, 39, and 27% of deaths in Nigeria, Pakistan, and Ethiopia, respectively. Under current treatment utilization patterns, 34, 42, and 30% of pneumonia deaths not averted by treatment would occur among the poorest quintile in each country (S2). When applying equal treatment utilization across quintiles (S3), we saw higher numbers of deaths averted while maintaining the distribution of these deaths (same distribution as S1). If, instead, we increased utilization among the poor (by setting proportionality to baseline CFR), we saw increases in the number of deaths averted by treatment and decreases in AUC (S4). This was especially visible in Pakistan since the baseline mortality risk there was much higher among the poor. Equalizing the baseline mortality risk first and then applying current quintile-specific treatment utilization would also lead to increases in the overall magnitude of averted deaths and decreases in AUC, but this would be less effective than S4 for all three countries.

Diarrhea

Among the three countries, only Ethiopia introduced RV in 2016 (Figure 4.4). Current vaccine coverage results in an increase in AUC as higher proportions of cases are averted among the richer quintiles (S2). Strategies of either distributing the vaccines in proportion to baseline risks (S4) or equalizing the risks prior to vaccines both increase the size of the total cases averted and decrease AUC (S5).

Current quintile-specific treatment utilization increases AUC in Ethiopia because 53% of those with diarrhea among the richest quintile seek care versus only 22% in the poorest quintile. If utilization patterns were proportional to CFR, we would see an increase in the total number of deaths averted by treatment and a reduction in AUC (S4). In the context of Ethiopia, this strategy would be more favorable than first setting equal CFR across quintiles while maintaining current utilization rates (S5).

4.6 Discussion

Equity is increasingly gaining attention on the global development agenda (2,4). To understand whether certain health interventions lead to changes in health equity, we developed an analytical approach to estimate the changes in the distribution of childhood disease-related incidence and mortality by income quintile with these interventions. We applied this approach to examine how vaccine programs affect health equity under different scenarios of intervention coverage and treatment utilization assumptions in LMICs.

Our study highlighted several factors that would substantially contribute to the unequal distribution of childhood disease. First, higher prevalence of risk factors, such as wasting, underweight and stunting, among the poor contribute to unequal distribution of childhood disease incidence, before any intervention (immunization or treatment) is even introduced. Second, large differences were observed in vaccine coverage across income quintiles. In many countries, vaccine coverage among the top two quintiles can be three-to-four times higher than among the bottom quintile. Third, unequal distribution of deaths was caused by the combination of unequal distribution of prognostic factors (hence an unequal case fatality ratio) and treatment utilization across quintiles. Our results

suggest that the most appropriate strategy to remedy childhood disease inequities for each country would depend on country context, namely how the baseline risks, current vaccine coverage and treatment utilization are distributed across socio-economic groups.

The Global Vaccine Action Plan listed equity as one of its six guiding principles in delivering universal access to immunization (12). It emphasized "equitable access to immunization" as a core component of the right to health, and suggested that closing the coverage gap between the lowest and highest wealth quintiles would lead to greater equity. However, as shown in this study, merely ensuring equal access to vaccines will not reduce the health outcomes gap across income quintiles (see scenario 3 in Figures 4.1-3). The poor face higher baseline risks which are tied to social determinants of health such as wealth and education, in addition to lower treatment utilization. In our study, we find that Scenario 4 (distributing vaccines proportional to baseline risk) yields the most equitable distribution of disease burden. The pursuit of health equity requires more than ensuring equal access to one intervention, rather, a more systemic approach in addressing the health gaps between subgroups is required.

This study makes an important contribution to the limited publications on the systematic assessment of the distributional burden of childhood diseases and of the distributional impact of vaccines (8,9,19). It builds on previous work and extends the analysis to a large number of countries and three childhood diseases and corresponding vaccines. Our methodology could in fact be extended in the future to examine the distribution of other diseases and the distributional impact of other health interventions, and across other population sub-groups (e.g. region, gender).

One potential application of this study is to provide inputs to decision-makers on how to determine appropriate equity-enhancing strategies for countries. We presented estimates for several realistic policy options, including providing equal vaccine coverage across quintiles, targeting the interventions toward the poor, and addressing the underlying risks before improving vaccine coverage. One key input required to determine strategies is costs. We do not have data on how much more it would cost to increase intervention coverage among the poor versus the rich, nor do we know how much effort it would take to address the inequities in the baseline morbidity and

mortality risks. Thus, while we can conclude from our study that certain scenarios are more effective than others, data on costs would be required to determine which scenario would be most cost-effective and sustainable under countries' budget constraints.

This study has several limitations. First, a key limitation lies in our simplification of disease progression. We assumed that whether one gets a disease solely depends on the prevalence and relative risk of risk factors and vaccine coverage. This paper does not involve a dynamic transmission model, thus does not reflect the potential nonlinear effects of vaccines on disease transmissibility and herd immunity. On a related note, we searched for risk factors related to crowding, household or neighborhood density as an attempt to account for the size of susceptible populations. Households in the poorest quintile are more likely to have more children, therefore disease transmission rate in this quintile may be higher than the richest quintile with fewer children. However, we were unable to find the relative risks of related risk factors and/or the prevalence of these risk factors by income quintile in DHS. Furthermore, non-specific effects of vaccines, such as their effect on overall mortality (20), as well as the timeliness of receiving the vaccines, were not taken into account. We believe including these factors would lead to a more skewed distribution of cases. Second, two other important modes of delivery for measles vaccination, measles second dose (MCV2) and supplementary immunization activities (SIA), was not included in the analysis due to lack of coverage data by quintile. Third, several assumptions were made for PCV and RV. We only focused on the effect of PCV on pneumococcal pneumonia and RV on rotavirus diarrhea, and did not account for additional benefits these vaccines may have on other antigens that may be distributed differently across quintiles. Similarly, pneumonia caused by viral infection and diarrhea caused by bacterial infections were not considered. Fourth, for some countries the DHS did not have complete data on the prevalence of risk and prognostic factors by income quintile, so we assumed they were at the same levels as neighboring or similar countries. Fifth, we were not able to validate the accuracy of the estimates since empirical data, especially for the counterfactual scenario, were not available. One alternative for verification would be to collect morbidity and mortality data at the subnational or national levels and examine the relationship between their respective income levels. This work points to these important data collection needs in the future.

Our findings contribute toward understanding how diseases and the benefits of health interventions might be distributed, specifically in relation to achieving Sustainable Development Goal 3 in ensuring essential health services are provided for all. Achieving equity in health outcomes will only occur in step by step processes, which is why this paper is important in illustrating the likely distributional results of different approaches. The outputs can provide decision makers with information on the likely distributional effects of policies, and thereby help promote more equitable resource allocation, even when empirical data are unavailable.

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4.9 Main Figures and Tables

Table 4.1. List of symbols used and corresponding parameters and data sources

Parameter definition	Symbol	Parameter value	Data source
Number of cases and deaths in income quintile i	C_i, D_i	--	Authors' estimation
Total number of attributable cases and deaths	TC_a, TD_a	--	(15,18)
Total number of unattributable cases and deaths	TC_{ua}, TDu_a	--	(15,18)
Proportion of attributable cases and deaths in quintile i	Ac_i, Ad_i	See Appendix S4.3	Authors' estimation
Proportion of attributable cases and deaths averted by vaccine in quintile i	$Ac_{v,i}$, $Ad_{v,i}$	See Appendix S4.3	Authors' estimation
Disease-specific relative risk of risk factor j or prognostic factor l	RR_j, RR_l	See Table 4.2	--
Relative weight assigned to risk factor j or prognostic factor l	w_j, u_l	--	Authors' estimation
Prevalence of risk factor j or prognostic factor l in quintile i	P_{ij}, P_{il}	See Table 4.2	--
Vaccine efficacy	E	MCV1: 0.85 PCV: 0.26 for radiologically confirmed pneumonia RV: 0.59 for rotavirus diarrhea cases	(21–23)
Case fatality ratio for quintile i Average case fatality ratio across quintiles	CFR_i CFR_{avg}	Differ by country	(15)
Healthcare treatment efficacy	Eff	Measles: 0.62 Pneumonia 0.70 Diarrhea: 0.93	(28,29,37)

MCV1: measles vaccine first dose; PCV: pneumococcal conjugate vaccine; RV: rotavirus vaccine.

Table 4.2. Risk and prognostic factors, and relative risks for morbidity and mortality, for measles, diarrhea and pneumonia

Risk factors with asterisks were not included in the analysis due to the following reasons:

*Demographic and Health Survey data unavailable by income quintile

**lower relative risk

***poor data quality and/or poor variable definition

SD: standard deviation

Disease-vaccine pair	Risk factors of morbidity (relative risk magnitude is indicated in parentheses)	Prognostic factors of mortality (relative risk magnitude is indicated in parentheses)	Sources
Measles – Measles vaccine	• Wasting: z-score < -3SD (38.0); -2SD < z-score < -3SD (8.5) • Maternal education (3.2)* • Having no other children vaccinated at home (3.0)* • Underweight: z-score < -3SD (5.7); -2SD < z-score < -3SD (2.5) • Stunting: z-score < -3SD (2.5); -2SD < z-score < -3SD (1.5) • Vitamin A deficiency (2.4)	• Wasting: z-score < -3SD (38.0); -2SD < z-score < -3SD (8.5) • Underweight: z-score < -3SD (5.7); -2SD < z-score < -3SD (2.5) • Stunting: z-score < -3SD (2.5); -2SD < z-score < -3SD (1.5) • Vitamin A deficiency (2.4) • More than one child (1.8)* • Age at infection (NA)* • Secondary (versus primary) exposure (NA)* • Infection with complication (NA)* • Overcrowding (NA)* • Intensity of exposure and patterns of disease transmission (NA)*	(23–26)
Pneumonia – Pneumococcal conjugate vaccine	• Wasting: z-score < -3SD (116.7); -2SD < z-score < -3SD (25.6) • Non-exclusive breastfeeding: None (4.5); Partial (5.4); Predominant (1.8) • Underweight: z-score < -3SD (2.1); -2SD < z-score < -3SD (1.3) • Stunting: z-score < -3SD (1.9); -2SD < z-score < -3SD (1.2)** • Zinc deficiency (1.8)* • Vitamin A deficiency (1.6) • Low birth weight (<2500g) (1.4) • Exposed to household air pollution (1.4)* • Crowding – more than five people per household (1.4)* • Secondhand smoke (1.2)* • Parental literacy level (NA)*	• Wasting: z-score < -3SD (116.7); -2SD < z-score < -3SD (25.6) • Non-exclusive breastfeeding: None (51.4); Partial (2.8); Predominant (1.9) • Zinc deficiency (1.7)* • Underweight: z-score < -3SD (2.1); -2SD < z-score < -3SD (1.3) • Stunting: z-score < -3SD (1.9); -2SD < z-score < -3SD (1.2) • Vitamin A deficiency (1.6) • Secondhand smoke (1.2)*	(15,16,23, 25,26)
Diarrhea –	• Wasting: z-score < -3SD (105.8); -2SD < z-score < -3SD (23.3)	• Wasting: z-score < -3SD (105.8); -2SD < z-score < -3SD	(15,23,25,

Rotavirus vaccine	• Unsafe water source (11.2)* • Unsafe sanitation (3.2) • Mothers handwashing not practiced at critical time (2.2)* • Underweight: z-score < -3SD (2.3); -2SD < z-score < -3SD (1.2) • Non-exclusive breastfeeding: None (2.2); Partial (1.5); Predominant (1.2) • Stunting: z-score < -3SD (1.9); -2SD < z-score < -3SD (1.2) • Zinc deficiency (1.9)* • No hand washing with soap (1.7)*** • Maternal literacy (1.7)* • Having more than two under five children (1.7)*	(23.3) • Unsafe water source (11.2)* • Non-exclusive breastfeeding: None (9.7); Partial (3.9); Predominant (2.1) • Unsafe sanitation (3.2) • Underweight; z-score < -3SD (2.3); -2SD < z-score < -3SD (1.2) • Zinc deficiency (2.0)* • Stunting: z-score < -3SD (1.9); -2SD < z-score < -3SD (1.2) • No handwashing with soap (1.7)*** • Vitamin A deficiency (1.5)**	27,28)

Figure 4.1. Flow diagram of the analytical approach

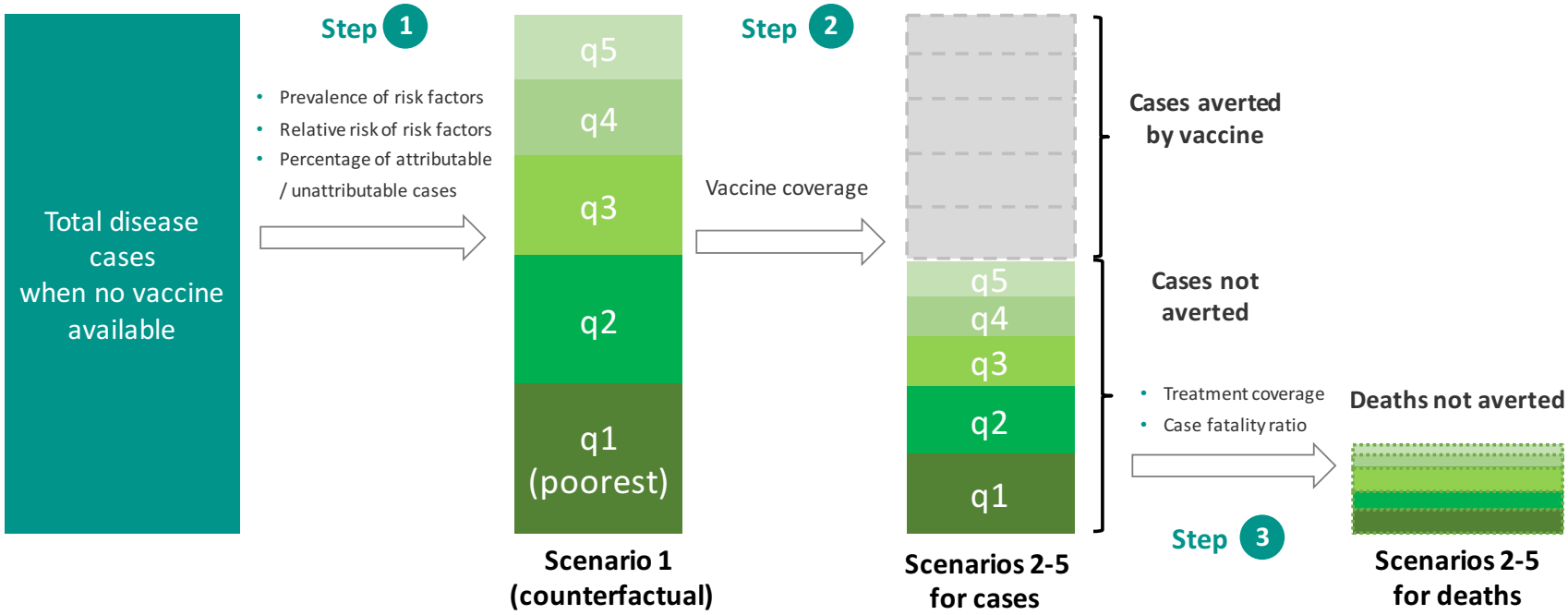
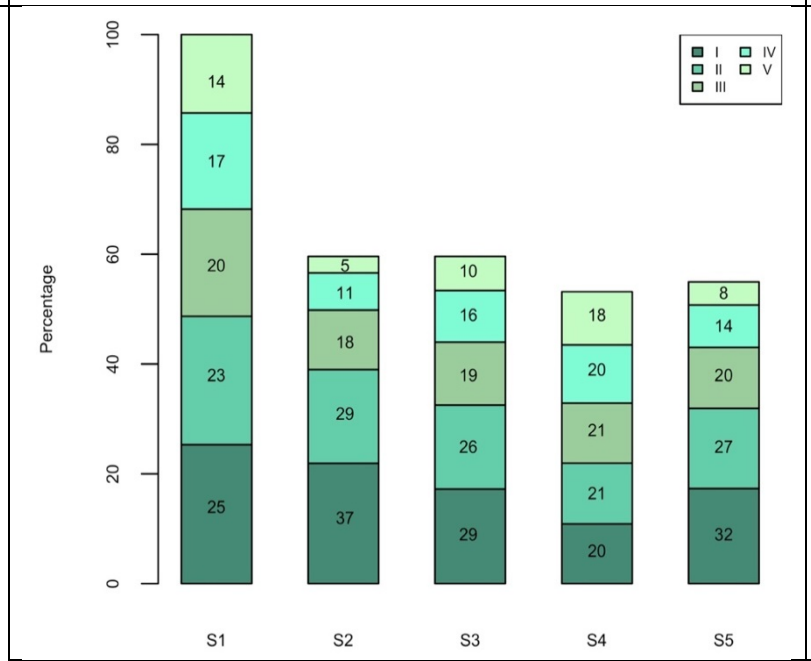
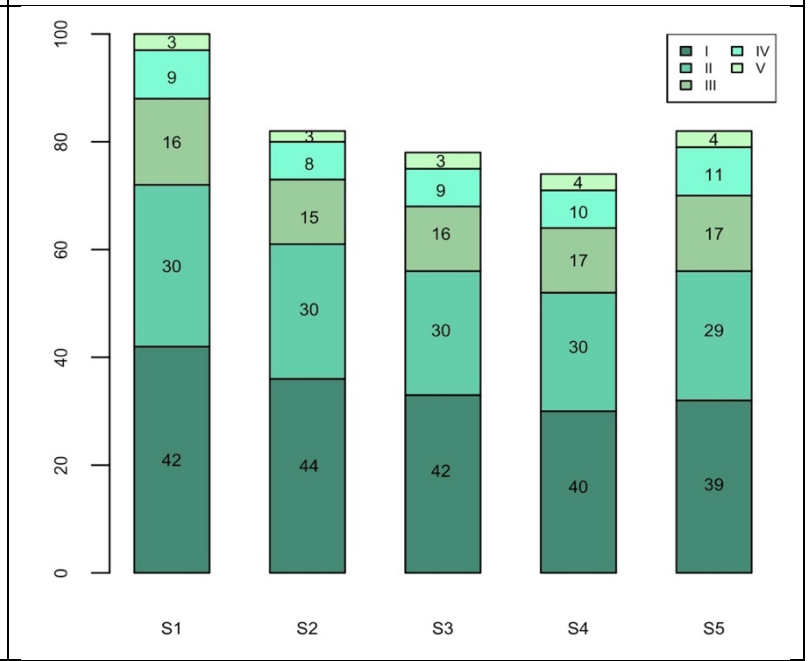


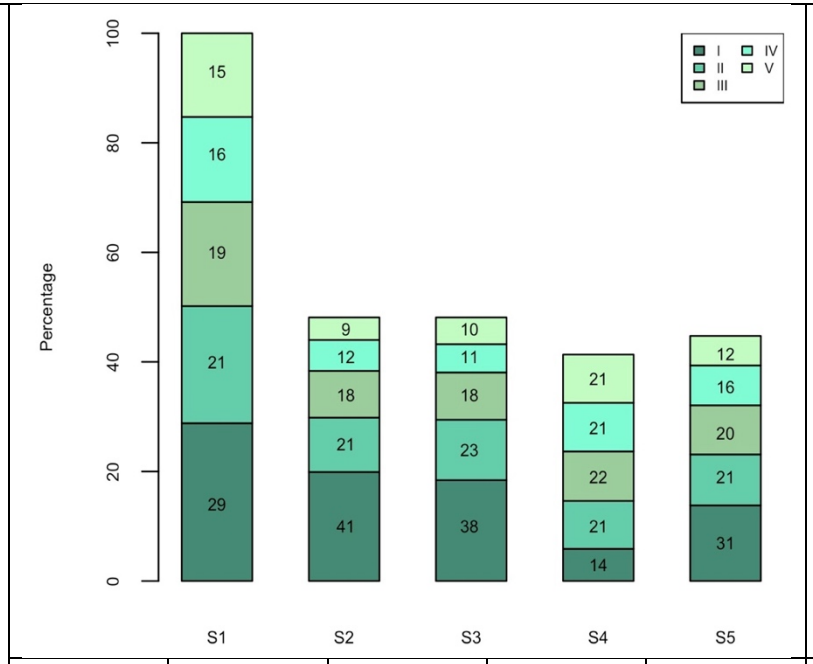
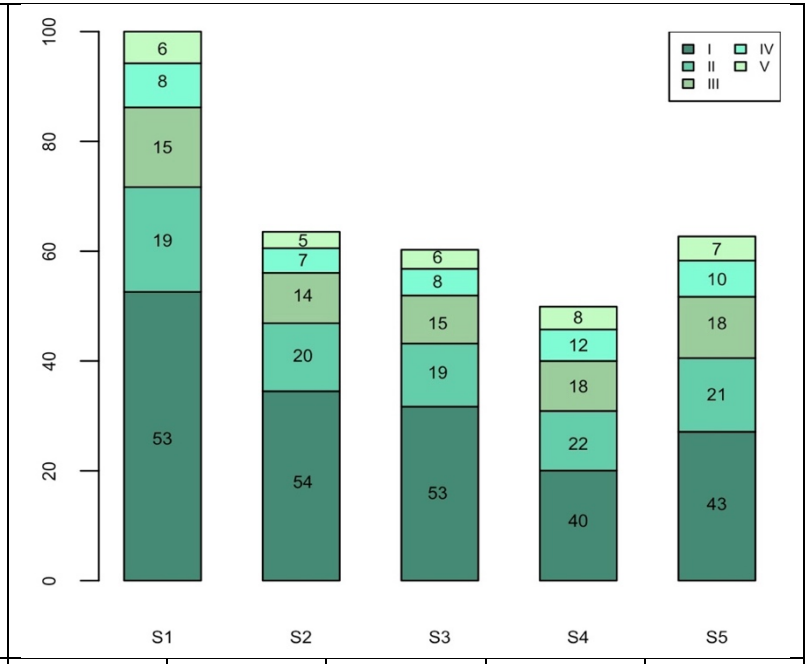
Figure 4.2. Distribution of measles cases and deaths by income quintile and scenario in Nigeria, Pakistan, and Ethiopia

The numbers in the green boxes represent the percentage of cases and deaths in each income quintile. I = Poorest, II = Poorer, III = Middle, IV = Richer, V = Richest. AUC = area under the curve. Δ AUC: Percent change in AUC compared to S1

Cases: Scenario 1 (S1): no vaccine program available; S2: current vaccine program; S3: total number of vaccines from S2 distributed equally across quintiles; S4: vaccine coverage proportional to quintile-specific baseline morbidity risks; S5: equal baseline morbidity risk with current quintile-specific vaccine coverage.

Deaths: S1: distribution of deaths among cases not averted by current vaccine programs with no treatment utilization; S2: current quintile-specific treatment utilization rates; S3: national average of utilization for all quintiles; S4: utilization rates proportional to quintile-specific baseline mortality risks; S5: equal baseline mortality risk with current quintile-specific treatment coverage rates.

	Cases					Deaths				
Nigeria										
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	40	40	47	45	-	18	22	26	19
Δ AUC (%)	-	+21	+8	-9	+13	-	+2	0	-3	-5

Pakistan									
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	52	52	59	55	-	36	40	50	37
Δ AUC (%)	-	+16	+15	-20	+3	-	+3	0	-12	-9

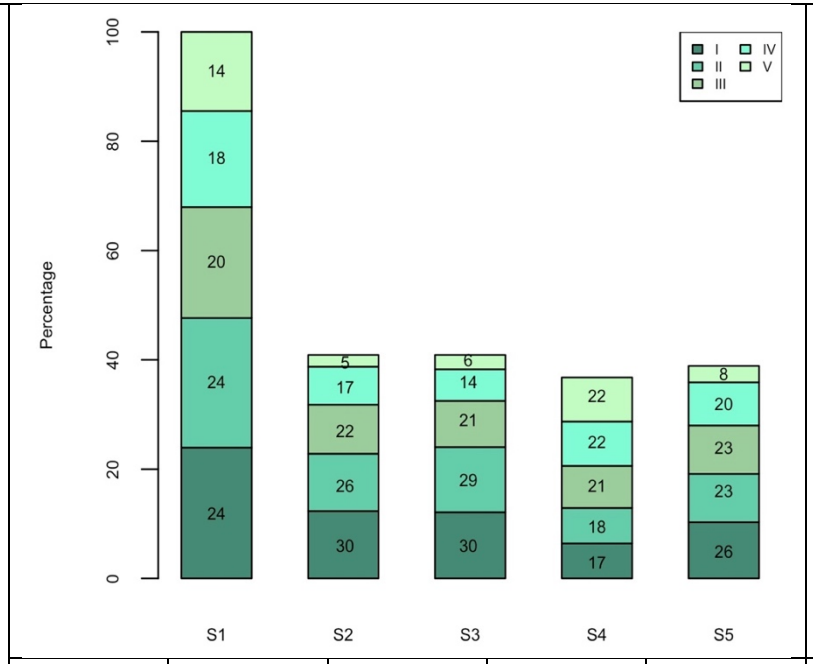
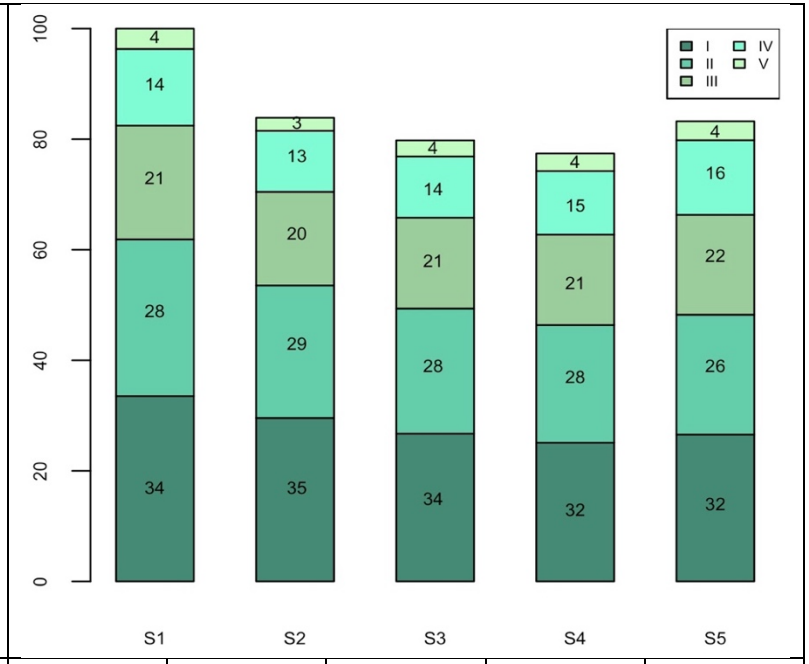
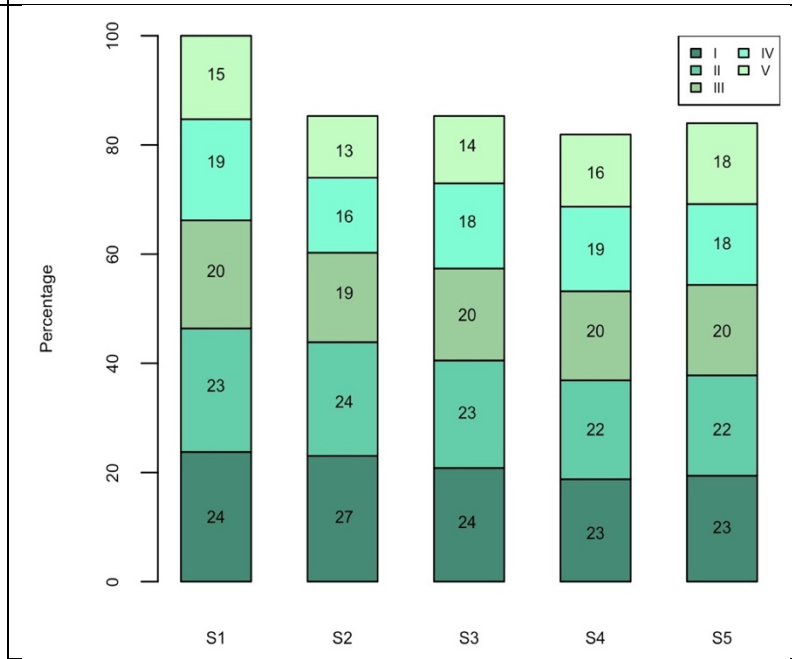
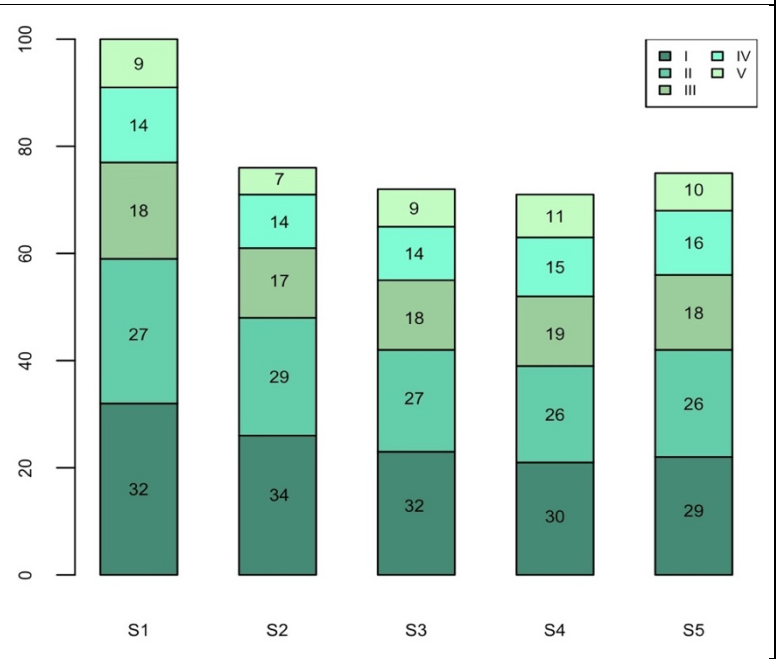
Ethiopia									
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	59	59	63	61	-	16	20	23	17
Δ AUC (%)	-	+13	+15	-16	+6	-	+2	0	-2	-4

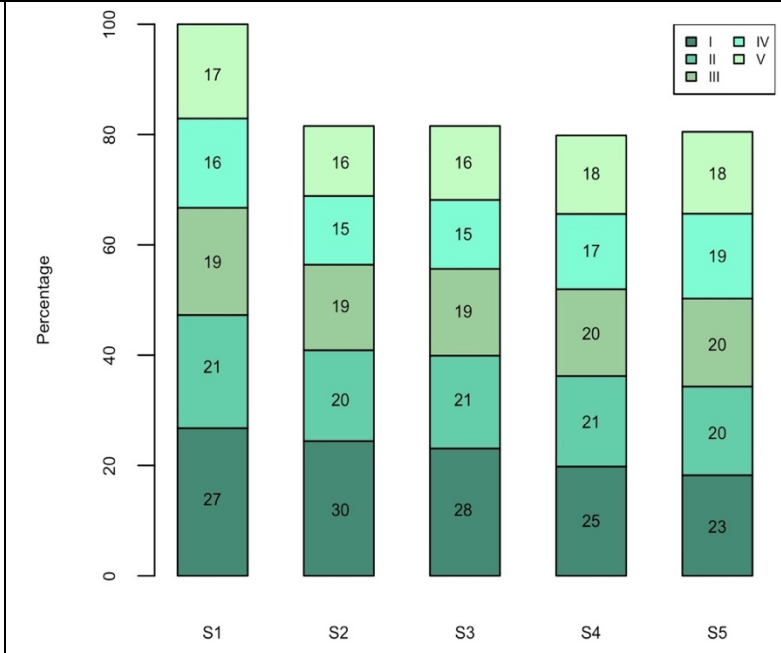
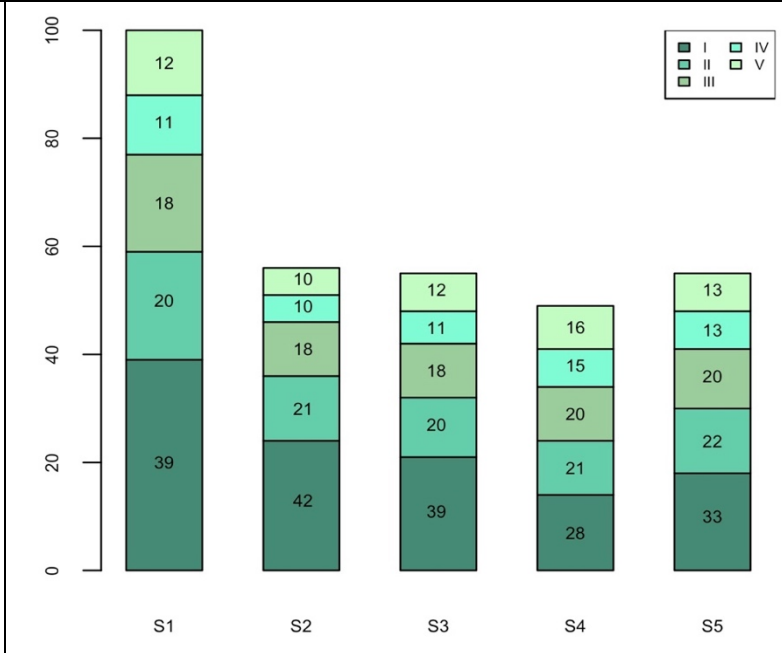
Figure 4.3. Distribution of pneumonia cases and deaths by income quintile and scenario in Nigeria, Pakistan, and Ethiopia

The numbers in the green boxes represent the percentage of cases and deaths in each income quintile. I = Poorest, II = Poorer, III = Middle, IV = Richer, V = Richest. AUC = area under the curve. Δ AUC: Percent change in AUC compared to S1

Cases: Scenario 1 (S1): no vaccine program available; S2: current vaccine program; S3: total number of vaccines from S2 distributed equally across quintiles; S4: vaccine coverage proportional to quintile-specific baseline morbidity risks; S5: equal baseline morbidity risk with current quintile-specific vaccine coverage rates.

Deaths: S1: distribution of deaths among cases not averted by current vaccine programs with no treatment utilization; S2: current treatment utilization provision; S3: national average of utilization for all quintiles; S4: treatment utilization rates proportional to quintile-specific baseline mortality risks; S5: equal baseline mortality risk with current quintile-specific treatment utilization rates.

	Cases					Deaths				
Nigeria										
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	15	15	18	16	-	24	28	30	26

Δ AUC (%)	-	+6	+1	-2	-2	-	+5	0	-3	-3
Pakistan								
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	18	18	20	20	-	44	46	51	45
Δ AUC (%)	-	+4	+2	-3	-6	-	+5	0	-12	-6

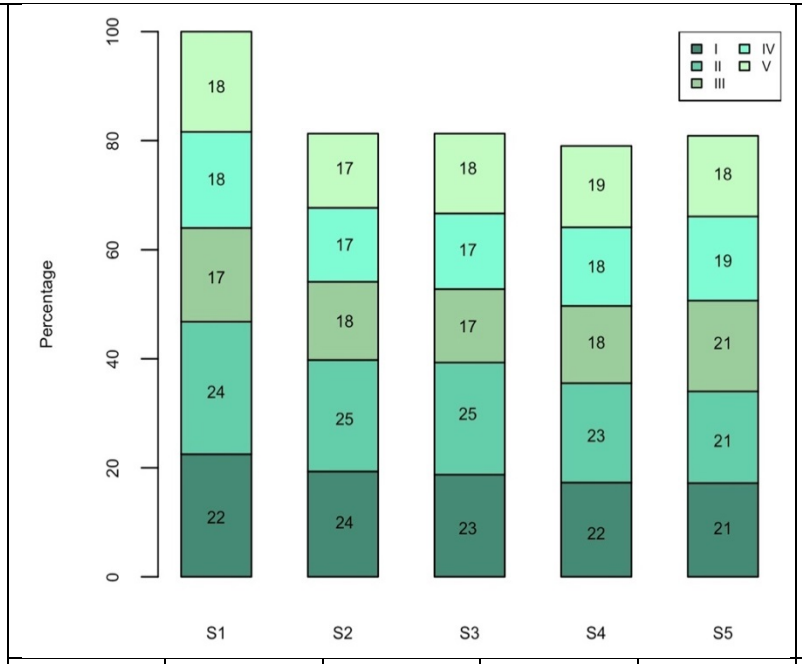
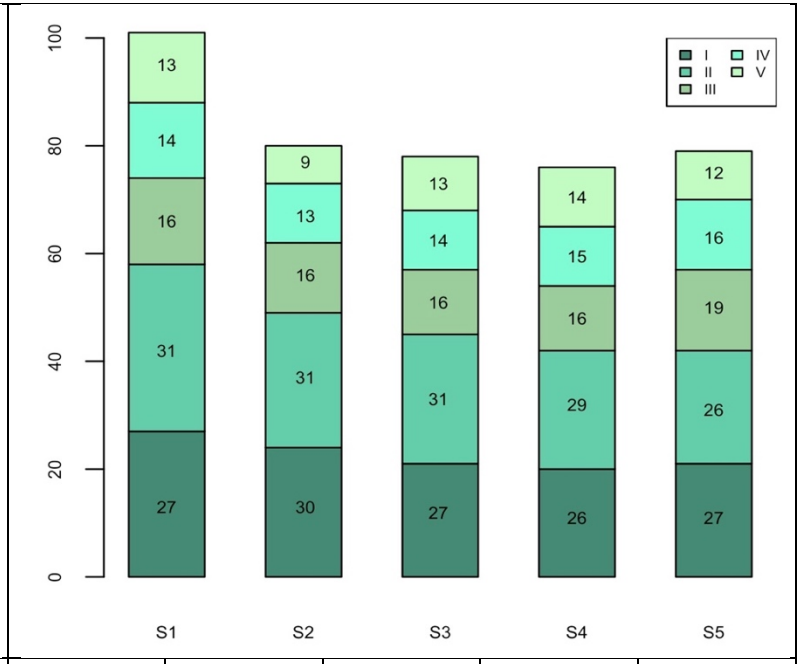
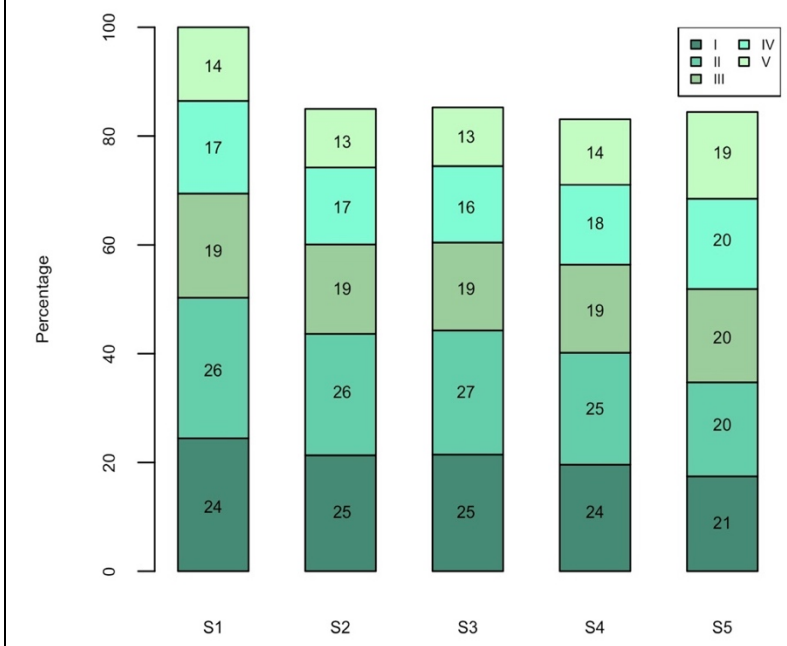
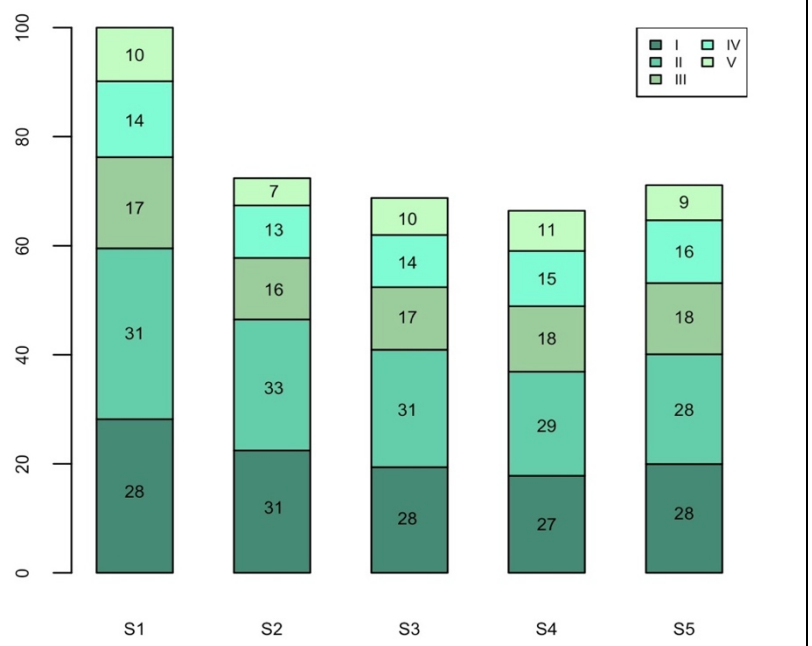
Ethiopia										
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	19	19	21	19	-	20	22	24	21
Δ AUC (%)	-	+3	+1	-2	-3	-	+6	0	-3	-2

Figure 4.4. Distribution of diarrhea cases and deaths by income quintile and scenario in Ethiopia

The numbers in the green boxes represent the percentage of cases and deaths in each income quintile. I = Poorest, II = Poorer, III = Middle, IV = Richer, V = Richest. AUC = area under the curve. Δ AUC: Percent change in AUC compared to S1

Cases: Scenario 1 (S1): no vaccine program available; S2: current vaccine program; S3: total number of vaccines from S2 distributed equally across quintiles; S4: vaccine coverage proportional to quintile-specific baseline morbidity risks; S5: equal baseline morbidity risk with current quintile-specific vaccine coverage rates.

Deaths: S1: distribution of deaths among cases not averted by current vaccine programs with no treatment utilization; S2: current treatment utilization provision; S3: national average of treatment utilization for all quintiles; S4: treatment utilization rates proportional to quintile-specific baseline mortality risks; S5: equal baseline mortality risk with current quintile-specific treatment utilization rates.

	Cases					Deaths				
Ethiopia										
	S1	S2	S3	S4	S5	S1	S2	S3	S4	S5
Total averted (%)	-	15	15	17	16	-	28	31	34	29
Δ AUC (%)	-	+2	+2	-2	-10	-	+6	0	-4	-2

4.10 Supplemental Material

S4.1. Country selection and Demographic and Health Survey year

We selected 41 low- and middle-income countries with Demographic and Health Surveys available after 2010, listed in Table S1 (1).

Table S4.1. List of 41 countries and Demographic and Health Survey year

Country	Year of Demographic and Health Survey
Armenia	2010
Bangladesh	2011
Benin	2011-12
Burkina Faso	2010
Burundi	2010
Cambodia	2014
Cameroon	2011
Chad	2014-15
Comoros	2012
Democratic Republic of the Congo	2013-14
Congo	2011-12
Côte d'Ivoire	2011-12
Ethiopia	2011
The Gambia	2013
Ghana	2014
Guinea	2012
Haiti	2012
Honduras	2011-12
Indonesia	2012
Kenya	2014
Kyrgyz Republic	2012
Lesotho	2014
Liberia	2013
Malawi	2010
Mali	2012-13
Mozambique	2011
Nepal	2011
Niger	2012
Nigeria	2013
Pakistan	2012-13
Rwanda	2010
Senegal	2014
Sierra Leone	2013
Tajikistan	2012
Tanzania	2010

Timor-Leste	2009-10
Togo	2013-14
Uganda	2011
Yemen	2013
Zambia	2013-14
Zimbabwe	2010-11

S4.2. Selection of risk and prognostic factors

We first searched the literature for risk and prognostic factors with the highest relative risks for diarrhea, measles, and pneumonia. For each factor, we also checked its availability by quintile-specific prevalence rate in the DHS (1). Factors that did not match with DHS variables, had poor data quality, or poor variable definition according to experts were excluded. We shortlisted five factors per disease (listed in the main paper, Table 4.2).

Prevalence rates by income quintile for malnutrition metrics (wasting, underweight, and stunting) and low birth weight were available in the DHS for most countries. Relative risk (RR) for each childhood malnutrition exposures is adjusted for the joint effect of the other malnutrition indicators, as described by the GBD 2013 Risk Factors Collaborators (2). We applied neighboring country data to countries with missing data.

Prevalence rates of vitamin A deficiency by income quintile were proxied with the percentage not given vitamin A supplements in the past six months among children aged 6 to 59 months. For countries missing this variable, we used the percentage who did not consumed foods rich in vitamin A in the past 24 hours among age 6 to 23 months as replacement.

For estimating the level of sanitation in one's household, we used the percentage of children whose stools were not disposed safely as a proxy.

For non-exclusive breastfeeding, the DHS provides data on the median duration (in months) of exclusive breastfeeding in the past three years by income quintile, and the national average (percentage) of exclusive breastfeeding among children of ages zero to five months and six months. To estimate the burden of non-exclusive breastfeeding, we assumed that the ratio of the average duration of exclusive breastfeeding of an income quintile to the national average is proportional to the ratio of the percentage of people exclusively breastfeeding in the same income quintile to the national average. The burden of non-exclusive breastfeeding is calculated as 100% minus the estimated prevalence of exclusive breastfeeding.

S4.3. Full results

Table S4.1 includes the distribution of cases and deaths for all 41 countries for the three vaccines (measles or MCV, pneumococcal conjugate vaccine or PCV, and rotavirus diarrhea or RV) for two scenarios.

For cases, scenario 1 (S1) assumes zero vaccine coverage; scenario 2 (S2) incorporates differences in current vaccine coverage across quintiles. For deaths among cases that were not averted by vaccine programs, S1 examines the distribution of deaths under the hypothetical scenario of people not having access to any care. S2 reflects the differences in the current treatment utilization rates across income quintiles.

Table S4.2 shows the area under the curve (AUC) of the cumulative percentage of cases and deaths by quintile for measles, pneumonia, and diarrhea in the 41 countries studied, by scenario. As illustrated in Figure S4.1, if cases and deaths are distributed equally across quintiles (i.e., 20% in each quintile), the AUC equals 250 (=5*100/2). Having an AUC greater than 250 (the area outside of the triangles) suggests that higher percentages of cases or deaths are in the poorer quintiles. The illustration shows a decrease in AUC after vaccine introduction (decrease in the area). On the other hand, an increase in the AUC between the two scenarios suggests that, among the remaining cases not averted by the program, a higher percentage of cases is among the poorer quintiles compared to prior vaccine introduction.

Figure S4.1. Illustration of the area under the curve

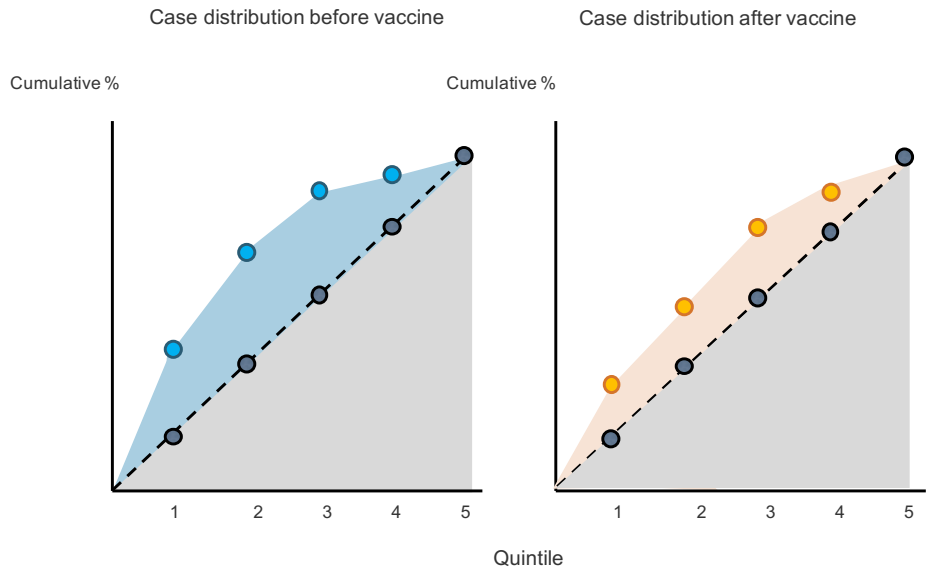


Table S4.1. Distribution of cases and deaths by income quintile for 41 countries for measles, pneumonia, and diarrhea

Quintile: 1: poorest, 2: poorer, 3: middle, 4: richer, 5: richest.
N/A: estimates not available due to no vaccine introduction in 2016.
Cases S1: distribution of cases under the assumption of zero vaccine coverage.
Cases S2: distribution of remaining cases after current vaccine coverage rates.
Deaths S1: distribution of remaining cases not averted by vaccine programs, under the hypothetical scenario of people not having access to any treatment.
Deaths S2: distribution of deaths with current treatment utilization rates.
MCV: measles first dose, PCV: pneumococcal conjugate vaccine, RV: rotavirus vaccine.

		MCV				PCV				RV			
Country	Quintile	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2
	1	0.25	0.26	0.34	0.35	0.29	0.30	0.41	0.43	0.33	0.34	0.46	0.50
	2	0.21	0.18	0.18	0.19	0.20	0.20	0.18	0.19	0.21	0.21	0.18	0.19
	3	0.19	0.17	0.15	0.15	0.17	0.17	0.12	0.12	0.15	0.15	0.10	0.10
	4	0.19	0.20	0.18	0.17	0.23	0.22	0.22	0.20	0.22	0.22	0.21	0.18
Armenia	5	0.16	0.18	0.15	0.13	0.12	0.11	0.07	0.06	0.09	0.09	0.05	0.04
	1	0.25	0.32	0.38	0.39	0.23	0.23	0.27	0.29	0.24	N/A	N/A	N/A
	2	0.22	0.21	0.22	0.22	0.21	0.21	0.22	0.24	0.22	N/A	N/A	N/A
	3	0.21	0.20	0.19	0.20	0.21	0.21	0.21	0.22	0.21	N/A	N/A	N/A
	4	0.17	0.15	0.12	0.12	0.17	0.17	0.15	0.13	0.17	N/A	N/A	N/A
Bangladesh	5	0.16	0.12	0.09	0.07	0.18	0.18	0.15	0.12	0.16	N/A	N/A	N/A
	1	0.24	0.30	0.35	0.38	0.25	0.26	0.32	0.35	0.26	N/A	N/A	N/A
	2	0.20	0.22	0.21	0.21	0.19	0.20	0.18	0.18	0.20	N/A	N/A	N/A
	3	0.22	0.20	0.21	0.19	0.22	0.21	0.23	0.20	0.23	N/A	N/A	N/A
	4	0.18	0.15	0.13	0.13	0.17	0.16	0.13	0.13	0.16	N/A	N/A	N/A
Benin	5	0.17	0.12	0.10	0.10	0.17	0.17	0.14	0.14	0.16	N/A	N/A	N/A
	1	0.24	0.31	0.36	0.39	0.22	0.23	0.26	0.31	0.24	0.34	0.27	0.31
	2	0.21	0.22	0.22	0.23	0.20	0.20	0.20	0.22	0.21	0.21	0.22	0.24
Burkina Faso	3	0.21	0.19	0.18	0.17	0.21	0.21	0.21	0.18	0.21	0.15	0.22	0.22

	4	0.19	0.15	0.14	0.13	0.19	0.19	0.18	0.17	0.19	0.22	0.18	0.14
	5	0.16	0.13	0.10	0.08	0.18	0.17	0.15	0.12	0.15	0.09	0.11	0.09
	1	0.24	0.28	0.33	0.33	0.22	0.22	0.25	0.26	0.23	0.34	0.26	0.27
	2	0.20	0.21	0.20	0.20	0.20	0.20	0.19	0.20	0.20	0.21	0.19	0.19
	3	0.21	0.20	0.20	0.19	0.19	0.19	0.19	0.18	0.20	0.15	0.20	0.18
	4	0.19	0.18	0.16	0.17	0.18	0.18	0.16	0.17	0.19	0.22	0.17	0.19
Burundi	5	0.16	0.14	0.11	0.10	0.21	0.21	0.21	0.20	0.18	0.09	0.18	0.17
	1	0.24	0.34	0.39	0.38	0.21	0.22	0.24	0.24	0.24	N/A	N/A	N/A
	2	0.22	0.26	0.27	0.27	0.19	0.20	0.20	0.21	0.22	N/A	N/A	N/A
	3	0.19	0.18	0.16	0.15	0.18	0.18	0.17	0.15	0.18	N/A	N/A	N/A
	4	0.19	0.12	0.11	0.11	0.19	0.19	0.18	0.19	0.19	N/A	N/A	N/A
Cambodia	5	0.16	0.10	0.08	0.08	0.22	0.22	0.21	0.21	0.17	N/A	N/A	N/A
	1	0.30	0.44	0.56	0.60	0.28	0.29	0.42	0.48	0.36	0.37	0.50	0.54
	2	0.23	0.25	0.23	0.22	0.22	0.22	0.23	0.21	0.24	0.24	0.24	0.23
	3	0.18	0.14	0.10	0.09	0.19	0.19	0.16	0.14	0.18	0.17	0.13	0.12
	4	0.16	0.11	0.07	0.06	0.16	0.16	0.11	0.10	0.13	0.12	0.08	0.07
Cameroon	5	0.13	0.06	0.04	0.03	0.15	0.12	0.08	0.07	0.10	0.09	0.05	0.04
	1	0.20	0.21	0.20	0.21	0.18	N/A	N/A	N/A	0.19	N/A	N/A	N/A
	2	0.19	0.20	0.19	0.20	0.19	N/A	N/A	N/A	0.20	N/A	N/A	N/A
	3	0.22	0.22	0.24	0.24	0.22	N/A	N/A	N/A	0.23	N/A	N/A	N/A
	4	0.22	0.23	0.25	0.24	0.21	N/A	N/A	N/A	0.21	N/A	N/A	N/A
Chad	5	0.17	0.14	0.12	0.11	0.20	N/A	N/A	N/A	0.17	N/A	N/A	N/A
	1	0.26	0.35	0.41	0.41	0.24	N/A	N/A	N/A	0.26	N/A	N/A	N/A
	2	0.22	0.24	0.24	0.25	0.21	N/A	N/A	N/A	0.20	N/A	N/A	N/A
	3	0.19	0.14	0.13	0.13	0.20	N/A	N/A	N/A	0.20	N/A	N/A	N/A
	4	0.19	0.14	0.12	0.11	0.19	N/A	N/A	N/A	0.18	N/A	N/A	N/A
Comoros	5	0.15	0.13	0.09	0.10	0.16	N/A	N/A	N/A	0.15	N/A	N/A	N/A
	1	0.25	0.36	0.42	0.44	0.21	0.22	0.25	0.28	0.26	0.27	0.31	0.33
	2	0.23	0.25	0.26	0.26	0.22	0.22	0.24	0.25	0.24	0.24	0.26	0.27
Congo	3	0.20	0.17	0.15	0.15	0.19	0.19	0.18	0.20	0.19	0.19	0.18	0.19

	4	0.18	0.13	0.10	0.09	0.20	0.19	0.18	0.15	0.17	0.17	0.14	0.14
	5	0.14	0.09	0.06	0.05	0.19	0.18	0.15	0.12	0.14	0.13	0.10	0.08
	1	0.25	0.30	0.37	0.40	0.21	0.23	0.25	0.30	0.25	0.25	0.30	0.32
	2	0.21	0.24	0.24	0.23	0.20	0.20	0.20	0.22	0.21	0.21	0.22	0.20
	3	0.20	0.20	0.18	0.17	0.20	0.20	0.20	0.17	0.20	0.20	0.19	0.20
	4	0.18	0.16	0.14	0.13	0.19	0.19	0.18	0.16	0.18	0.18	0.16	0.15
Côte d'Ivoire	5	0.16	0.10	0.08	0.07	0.19	0.18	0.17	0.16	0.16	0.16	0.13	0.13
	1	0.25	0.31	0.34	0.35	0.22	0.23	0.26	0.27	0.24	N/A	N/A	N/A
	2	0.24	0.26	0.29	0.29	0.23	0.24	0.28	0.28	0.25	N/A	N/A	N/A
	3	0.22	0.21	0.21	0.20	0.21	0.21	0.22	0.21	0.22	N/A	N/A	N/A
Democratic Republic of the Congo	4	0.17	0.15	0.12	0.12	0.18	0.18	0.15	0.15	0.17	N/A	N/A	N/A
	5	0.11	0.07	0.04	0.04	0.15	0.14	0.09	0.09	0.12	N/A	N/A	N/A
	1	0.24	0.30	0.34	0.35	0.22	0.24	0.27	0.30	0.24	0.25	0.28	0.31
	2	0.24	0.26	0.28	0.28	0.24	0.25	0.31	0.31	0.26	0.26	0.31	0.33
	3	0.20	0.22	0.21	0.20	0.17	0.18	0.16	0.16	0.19	0.19	0.17	0.16
	4	0.18	0.17	0.14	0.13	0.18	0.17	0.14	0.13	0.17	0.17	0.14	0.13
Ethiopia	5	0.14	0.05	0.04	0.03	0.18	0.17	0.13	0.09	0.14	0.13	0.10	0.07
	1	0.20	0.17	0.17	0.17	0.18	0.18	0.16	0.15	0.18	0.18	0.16	0.16
	2	0.21	0.19	0.20	0.19	0.19	0.19	0.19	0.19	0.20	0.20	0.19	0.18
	3	0.23	0.21	0.24	0.24	0.24	0.24	0.29	0.28	0.24	0.24	0.29	0.29
	4	0.19	0.17	0.16	0.17	0.20	0.20	0.19	0.21	0.19	0.19	0.19	0.20
The Gambia	5	0.17	0.27	0.23	0.24	0.18	0.19	0.17	0.17	0.18	0.18	0.17	0.17
	1	0.25	0.28	0.34	0.32	0.21	0.21	0.25	0.24	0.25	0.25	0.29	0.25
	2	0.21	0.21	0.21	0.21	0.19	0.20	0.20	0.20	0.21	0.21	0.21	0.21
	3	0.17	0.17	0.14	0.15	0.17	0.17	0.14	0.15	0.17	0.17	0.14	0.17
	4	0.20	0.21	0.20	0.21	0.21	0.21	0.22	0.22	0.20	0.20	0.20	0.21
Ghana	5	0.17	0.14	0.11	0.11	0.21	0.21	0.20	0.20	0.17	0.17	0.16	0.16
	1	0.25	0.30	0.35	0.38	0.25	N/A	N/A	N/A	0.28	N/A	N/A	N/A
	2	0.23	0.21	0.23	0.23	0.20	N/A	N/A	N/A	0.21	N/A	N/A	N/A
Guinea	3	0.22	0.22	0.22	0.21	0.21	N/A	N/A	N/A	0.22	N/A	N/A	N/A

	4	0.18	0.17	0.15	0.13	0.19	N/A	N/A	N/A	0.17	N/A	N/A	N/A
	5	0.13	0.09	0.06	0.04	0.15	N/A	N/A	N/A	0.11	N/A	N/A	N/A
	1	0.22	0.22	0.24	0.26	0.20	0.20	0.21	0.24	0.24	0.25	0.27	0.29
	2	0.21	0.21	0.21	0.22	0.20	0.20	0.20	0.22	0.22	0.22	0.23	0.25
	3	0.20	0.19	0.19	0.19	0.19	0.19	0.18	0.19	0.19	0.19	0.17	0.17
	4	0.20	0.21	0.21	0.19	0.24	0.24	0.28	0.25	0.23	0.22	0.24	0.23
Haiti	5	0.17	0.17	0.15	0.14	0.17	0.17	0.13	0.11	0.12	0.12	0.08	0.07
	1	0.23	0.21	0.24	0.25	0.16	0.16	0.14	0.15	0.23	0.23	0.21	0.21
	2	0.20	0.20	0.20	0.20	0.19	0.19	0.19	0.20	0.20	0.20	0.20	0.20
	3	0.20	0.21	0.21	0.21	0.22	0.22	0.24	0.24	0.21	0.21	0.22	0.23
	4	0.19	0.21	0.20	0.19	0.21	0.21	0.21	0.21	0.18	0.18	0.18	0.17
Honduras	5	0.19	0.17	0.16	0.15	0.22	0.22	0.22	0.20	0.19	0.19	0.19	0.19
	1	0.24	0.27	0.32	0.35	0.22	N/A	N/A	N/A	0.24	N/A	N/A	N/A
	2	0.22	0.23	0.24	0.23	0.22	N/A	N/A	N/A	0.22	N/A	N/A	N/A
	3	0.19	0.16	0.15	0.14	0.16	N/A	N/A	N/A	0.17	N/A	N/A	N/A
	4	0.19	0.19	0.18	0.17	0.21	N/A	N/A	N/A	0.20	N/A	N/A	N/A
Indonesia	5	0.16	0.14	0.11	0.11	0.19	N/A	N/A	N/A	0.16	N/A	N/A	N/A
	1	0.25	0.32	0.38	0.38	0.24	0.24	0.29	0.30	0.27	0.27	0.34	0.32
	2	0.22	0.22	0.22	0.22	0.20	0.20	0.21	0.20	0.20	0.20	0.20	0.20
	3	0.20	0.20	0.19	0.19	0.22	0.22	0.24	0.24	0.21	0.21	0.22	0.23
	4	0.17	0.14	0.12	0.12	0.16	0.16	0.13	0.14	0.16	0.16	0.13	0.13
Kenya	5	0.15	0.13	0.10	0.09	0.17	0.16	0.13	0.11	0.15	0.15	0.12	0.12
	1	0.22	0.19	0.21	0.22	0.19	0.19	0.19	0.20	0.23	N/A	N/A	N/A
	2	0.19	0.18	0.17	0.19	0.22	0.21	0.22	0.24	0.19	N/A	N/A	N/A
	3	0.20	0.20	0.20	0.22	0.20	0.20	0.20	0.23	0.21	N/A	N/A	N/A
	4	0.19	0.23	0.22	0.21	0.20	0.20	0.20	0.19	0.19	N/A	N/A	N/A
Kyrgyz Republic	5	0.20	0.20	0.20	0.16	0.19	0.19	0.19	0.14	0.18	N/A	N/A	N/A
	1	0.25	0.27	0.32	0.32	0.23	0.23	0.28	0.29	0.29	N/A	N/A	N/A
	2	0.23	0.27	0.30	0.29	0.21	0.21	0.23	0.22	0.24	N/A	N/A	N/A
Lesotho	3	0.19	0.14	0.13	0.13	0.19	0.18	0.17	0.17	0.18	N/A	N/A	N/A

	4	0.18	0.17	0.15	0.15	0.19	0.19	0.17	0.17	0.16	N/A	N/A	N/A
	5	0.15	0.15	0.11	0.10	0.18	0.19	0.15	0.15	0.13	N/A	N/A	N/A
	1	0.24	0.27	0.30	0.31	0.22	0.22	0.25	0.26	0.23	0.24	0.27	0.28
	2	0.22	0.22	0.24	0.24	0.19	0.19	0.20	0.18	0.21	0.21	0.21	0.22
	3	0.21	0.21	0.21	0.19	0.20	0.20	0.20	0.18	0.21	0.21	0.21	0.18
	4	0.17	0.17	0.14	0.15	0.19	0.19	0.18	0.19	0.18	0.18	0.16	0.17
Liberia	5	0.16	0.14	0.11	0.11	0.20	0.19	0.17	0.19	0.17	0.17	0.15	0.15
	1	0.25	0.27	0.33	0.34	0.26	0.26	0.34	0.37	0.29	0.29	0.37	0.36
	2	0.22	0.22	0.23	0.24	0.23	0.23	0.24	0.25	0.23	0.23	0.24	0.24
	3	0.21	0.21	0.21	0.20	0.21	0.21	0.21	0.19	0.22	0.22	0.21	0.22
	4	0.18	0.16	0.14	0.13	0.15	0.15	0.11	0.10	0.15	0.15	0.10	0.10
Malawi	5	0.14	0.13	0.09	0.09	0.15	0.15	0.10	0.09	0.12	0.12	0.07	0.08
	1	0.24	0.31	0.34	0.36	0.23	0.24	0.28	0.31	0.25	0.25	0.29	0.33
	2	0.24	0.25	0.28	0.28	0.23	0.23	0.26	0.27	0.24	0.24	0.27	0.26
	3	0.22	0.23	0.22	0.22	0.21	0.21	0.22	0.22	0.22	0.22	0.23	0.23
	4	0.16	0.13	0.10	0.09	0.17	0.16	0.13	0.11	0.15	0.15	0.11	0.10
Mali	5	0.14	0.09	0.06	0.05	0.16	0.15	0.12	0.09	0.14	0.14	0.10	0.08
	1	0.29	0.34	0.43	0.44	0.27	0.28	0.37	0.39	0.31	0.31	0.41	0.43
	2	0.23	0.27	0.26	0.28	0.23	0.23	0.25	0.27	0.22	0.22	0.23	0.26
	3	0.21	0.22	0.19	0.18	0.21	0.21	0.20	0.18	0.20	0.20	0.19	0.17
	4	0.15	0.10	0.07	0.07	0.15	0.15	0.10	0.10	0.15	0.14	0.10	0.08
Mozambique	5	0.12	0.07	0.04	0.04	0.14	0.13	0.08	0.07	0.12	0.12	0.07	0.06
	1	0.25	0.27	0.32	0.33	0.20	0.20	0.22	0.24	0.23	N/A	N/A	N/A
	2	0.22	0.24	0.24	0.24	0.19	0.19	0.18	0.18	0.21	N/A	N/A	N/A
	3	0.21	0.24	0.24	0.23	0.21	0.21	0.23	0.22	0.22	N/A	N/A	N/A
	4	0.19	0.16	0.14	0.14	0.21	0.20	0.21	0.19	0.20	N/A	N/A	N/A
Nepal	5	0.13	0.09	0.06	0.06	0.20	0.19	0.17	0.16	0.14	N/A	N/A	N/A
	1	0.25	0.29	0.34	0.37	0.25	0.26	0.32	0.37	0.26	0.27	0.33	0.38
	2	0.20	0.21	0.20	0.20	0.19	0.19	0.18	0.20	0.19	0.19	0.18	0.16
Niger	3	0.22	0.24	0.25	0.23	0.23	0.23	0.25	0.22	0.23	0.23	0.25	0.23

	4	0.18	0.15	0.13	0.13	0.16	0.16	0.13	0.13	0.16	0.15	0.12	0.12
	5	0.16	0.11	0.08	0.07	0.17	0.16	0.13	0.09	0.17	0.16	0.13	0.11
	1	0.26	0.37	0.42	0.44	0.24	0.27	0.32	0.34	0.25	N/A	N/A	N/A
	2	0.23	0.29	0.30	0.30	0.23	0.24	0.27	0.29	0.23	N/A	N/A	N/A
	3	0.19	0.18	0.16	0.15	0.20	0.19	0.18	0.17	0.20	N/A	N/A	N/A
	4	0.17	0.11	0.09	0.08	0.19	0.16	0.14	0.14	0.18	N/A	N/A	N/A
Nigeria	5	0.14	0.05	0.03	0.03	0.15	0.13	0.09	0.07	0.14	N/A	N/A	N/A
	1	0.29	0.41	0.53	0.55	0.27	0.30	0.39	0.42	0.28	N/A	N/A	N/A
	2	0.22	0.21	0.19	0.20	0.21	0.20	0.20	0.21	0.22	N/A	N/A	N/A
	3	0.19	0.18	0.14	0.14	0.19	0.19	0.18	0.18	0.21	N/A	N/A	N/A
	4	0.16	0.12	0.08	0.07	0.16	0.15	0.11	0.10	0.15	N/A	N/A	N/A
Pakistan	5	0.15	0.08	0.05	0.04	0.17	0.16	0.12	0.10	0.15	N/A	N/A	N/A
	1	0.23	0.25	0.28	0.31	0.23	0.23	0.27	0.30	0.24	0.24	0.28	0.35
	2	0.22	0.25	0.27	0.26	0.22	0.22	0.24	0.24	0.23	0.23	0.26	0.24
	3	0.19	0.20	0.18	0.18	0.12	0.12	0.09	0.09	0.15	0.15	0.11	0.10
	4	0.19	0.17	0.15	0.15	0.20	0.20	0.18	0.20	0.19	0.19	0.17	0.16
Rwanda	5	0.16	0.14	0.12	0.10	0.23	0.23	0.22	0.16	0.18	0.18	0.17	0.15
	1	0.25	0.26	0.32	0.32	0.22	0.22	0.25	0.24	0.24	0.24	0.26	0.27
	2	0.21	0.22	0.23	0.23	0.20	0.20	0.20	0.21	0.20	0.20	0.20	0.18
	3	0.20	0.21	0.20	0.20	0.21	0.21	0.22	0.21	0.21	0.21	0.21	0.22
	4	0.18	0.17	0.15	0.15	0.20	0.19	0.18	0.17	0.19	0.19	0.18	0.20
Senegal	5	0.15	0.14	0.10	0.11	0.18	0.18	0.15	0.17	0.17	0.17	0.15	0.13
	1	0.20	0.19	0.18	0.19	0.19	0.19	0.18	0.19	0.20	0.20	0.20	0.20
	2	0.23	0.24	0.28	0.29	0.22	0.22	0.25	0.25	0.24	0.24	0.27	0.32
	3	0.21	0.22	0.23	0.21	0.20	0.20	0.21	0.20	0.21	0.21	0.21	0.17
	4	0.19	0.19	0.18	0.18	0.19	0.19	0.18	0.19	0.19	0.18	0.17	0.16
Sierra Leone	5	0.16	0.16	0.13	0.13	0.19	0.20	0.18	0.17	0.17	0.17	0.15	0.14
	1	0.23	0.25	0.28	0.30	0.22	N/A	N/A	N/A	0.23	0.23	0.26	0.29
	2	0.20	0.18	0.17	0.19	0.18	N/A	N/A	N/A	0.19	0.19	0.17	0.20
Tajikistan	3	0.18	0.18	0.16	0.14	0.18	N/A	N/A	N/A	0.17	0.17	0.15	0.12

	4	0.21	0.19	0.20	0.19	0.22	N/A	N/A	N/A	0.22	0.22	0.24	0.22
	5	0.19	0.20	0.18	0.18	0.20	N/A	N/A	N/A	0.18	0.19	0.18	0.18
	1	0.25	0.28	0.34	0.34	0.21	0.22	0.25	0.26	0.25	0.25	0.29	0.29
	2	0.21	0.22	0.22	0.22	0.18	0.18	0.17	0.17	0.19	0.19	0.18	0.18
	3	0.20	0.23	0.21	0.23	0.20	0.20	0.20	0.21	0.20	0.20	0.20	0.23
	4	0.18	0.14	0.12	0.12	0.19	0.19	0.17	0.17	0.17	0.17	0.16	0.16
Tanzania	5	0.17	0.13	0.11	0.10	0.22	0.21	0.21	0.18	0.18	0.18	0.17	0.14
	1	0.23	0.31	0.34	0.36	0.22	N/A	N/A	N/A	0.24	N/A	N/A	N/A
	2	0.21	0.23	0.24	0.24	0.19	N/A	N/A	N/A	0.20	N/A	N/A	N/A
	3	0.21	0.19	0.20	0.18	0.21	N/A	N/A	N/A	0.22	N/A	N/A	N/A
	4	0.19	0.13	0.12	0.13	0.19	N/A	N/A	N/A	0.19	N/A	N/A	N/A
Timor-Leste	5	0.16	0.13	0.10	0.09	0.18	N/A	N/A	N/A	0.16	N/A	N/A	N/A
	1	0.23	0.22	0.24	0.24	0.22	0.22	0.25	0.26	0.26	0.26	0.30	0.27
	2	0.23	0.27	0.30	0.30	0.22	0.22	0.23	0.22	0.23	0.24	0.26	0.28
	3	0.22	0.26	0.27	0.28	0.22	0.22	0.24	0.26	0.23	0.23	0.25	0.26
	4	0.19	0.16	0.14	0.13	0.20	0.20	0.19	0.19	0.18	0.18	0.15	0.14
Togo	5	0.13	0.09	0.06	0.05	0.14	0.14	0.09	0.07	0.10	0.09	0.05	0.04
	1	0.21	0.22	0.23	0.23	0.19	0.19	0.18	0.18	0.21	0.21	0.22	0.21
	2	0.21	0.24	0.25	0.24	0.22	0.22	0.24	0.24	0.23	0.23	0.26	0.25
	3	0.22	0.23	0.24	0.24	0.19	0.20	0.20	0.20	0.20	0.20	0.19	0.18
	4	0.20	0.19	0.18	0.18	0.21	0.21	0.22	0.23	0.21	0.21	0.21	0.21
Uganda	5	0.16	0.13	0.11	0.11	0.19	0.19	0.16	0.15	0.14	0.14	0.12	0.14
	1	0.28	0.36	0.44	0.45	0.25	0.27	0.34	0.35	0.27	0.28	0.35	0.37
	2	0.22	0.25	0.25	0.25	0.21	0.22	0.22	0.23	0.22	0.22	0.23	0.23
	3	0.19	0.18	0.15	0.15	0.18	0.18	0.15	0.15	0.18	0.18	0.15	0.15
	4	0.17	0.14	0.10	0.10	0.18	0.17	0.15	0.15	0.17	0.17	0.15	0.14
Yemen	5	0.14	0.08	0.05	0.05	0.17	0.16	0.13	0.12	0.16	0.15	0.12	0.11
	1	0.25	0.28	0.34	0.35	0.23	0.24	0.28	0.29	0.25	0.25	0.30	0.31
	2	0.20	0.23	0.22	0.22	0.19	0.19	0.17	0.19	0.19	0.19	0.18	0.18
Zambia	3	0.19	0.19	0.18	0.18	0.18	0.19	0.17	0.18	0.19	0.19	0.17	0.16

	4	0.20	0.17	0.16	0.16	0.21	0.20	0.21	0.20	0.21	0.20	0.20	0.19
	5	0.16	0.12	0.10	0.09	0.19	0.19	0.17	0.14	0.17	0.17	0.15	0.16
	1	0.23	0.24	0.27	0.26	0.23	0.24	0.27	0.26	0.26	0.26	0.31	0.31
	2	0.22	0.26	0.27	0.28	0.22	0.23	0.25	0.26	0.23	0.24	0.26	0.26
	3	0.20	0.25	0.24	0.24	0.19	0.19	0.17	0.16	0.19	0.18	0.17	0.18
	4	0.20	0.14	0.13	0.13	0.21	0.21	0.21	0.21	0.20	0.20	0.19	0.19
Zimbabwe	5	0.16	0.12	0.09	0.09	0.14	0.14	0.10	0.11	0.12	0.12	0.07	0.07

Table S4.2. Area under the curve for measles, pneumonia, and diarrhea cases and deaths in 41 countries, by scenario

Quintile: 1: poorest, 2: poorer, 3: middle, 4: richer, 5: richest.
N/A: estimates not available due to no vaccine introduction in 2016.
Cases S1: distribution of cases under the assumption of zero vaccine coverage.
Cases S2: distribution of remaining cases after current vaccine coverage rates
Deaths S1: distribution of remaining cases not averted by vaccine programs, under the hypothetical scenario of people not having access to any treatment.
Deaths S2: distribution of deaths with current treatment utilization rates.
MCV: measles first dose, PCV: pneumococcal conjugate vaccine, RV: rotavirus vaccine.

	MCV				PCV				RV			
	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2
Armenia	272	264	287	296	283	284	315	324	298	298	331	343
Bangladesh	273	297	318	325	264	266	282	295	272	N/A	N/A	N/A
Benin	267	293	309	314	268	272	291	298	274	N/A	N/A	N/A
Burkina Faso	269	294	311	322	261	262	276	294	270	271	287	304
Burundi	270	280	299	300	253	253	261	264	260	260	269	270
Cambodia	269	311	327	325	247	251	258	258	265	N/A	N/A	N/A
Cameroon	292	340	371	378	281	290	331	343	314	318	356	366
Chad	252	260	260	267	246	N/A	N/A	N/A	254	N/A	N/A	N/A
Comoros	274	304	327	326	268	N/A	N/A	N/A	274	N/A	N/A	N/A
Congo	276	317	338	344	257	262	278	294	281	284	305	314
Côte d'Ivoire	272	297	317	324	254	260	269	283	271	273	288	294
Democratic Republic of the Congo	285	309	328	329	268	274	296	299	282	N/A	N/A	N/A
Ethiopia	276	308	324	330	265	273	294	309	281	284	304	318
The Gambia	258	231	241	239	248	247	248	245	250	250	248	245
Ghana	268	279	298	292	248	249	258	255	267	268	277	267
Guinea	279	296	316	327	270	N/A	N/A	N/A	288	N/A	N/A	N/A
Haiti	260	259	267	277	252	253	258	272	274	276	286	297

Honduras	259	256	266	269	236	236	233	240	260	260	257	257
Indonesia	269	280	299	303	257	N/A	N/A	N/A	269	N/A	N/A	N/A
Kenya	274	295	317	317	269	270	290	294	277	278	302	296
Kyrgyz Republic	254	243	247	260	252	250	253	269	261	N/A	N/A	N/A
Lesotho	275	285	308	307	262	262	281	283	289	N/A	N/A	N/A
Liberia	271	282	300	300	253	256	268	264	267	268	278	282
Malawi	276	284	306	309	280	281	312	321	293	293	323	320
Mali	278	306	324	332	269	275	296	310	280	282	304	315
Mozambique	290	320	347	352	283	287	322	331	295	297	330	342
Nepal	276	292	311	314	249	251	258	264	270	N/A	N/A	N/A
Niger	269	292	308	318	268	273	292	313	272	275	295	306
Nigeria	279	331	350	355	271	286	307	319	275	N/A	N/A	N/A
Pakistan	284	325	356	363	274	284	313	326	284	N/A	N/A	N/A
Rwanda	268	279	295	303	252	253	265	283	266	267	280	296
Senegal	273	281	302	301	257	258	271	267	264	265	273	275
Sierra Leone	261	259	269	273	252	251	257	261	261	261	268	278
Tajikistan	256	260	267	272	250	N/A	N/A	N/A	257	256	259	269
Tanzania	270	287	305	307	248	250	257	267	266	267	275	282
Timor-Leste	266	296	309	314	259	N/A	N/A	N/A	267	N/A	N/A	N/A
Togo	275	288	302	304	267	268	286	291	288	288	310	309
Uganda	262	272	281	280	251	251	257	259	267	266	275	269
Yemen	282	316	342	345	268	275	299	303	277	281	305	311
Zambia	267	288	304	307	255	258	269	278	265	266	278	279
Zimbabwe	267	286	299	298	269	272	289	285	282	283	304	305

S4.4. Sensitivity analyses

Three sets of sensitivity analyses were performed.

Sensitivity analysis 1. *Accounting for differences in the sizes of the under-five population in each quintile.*

I adjusted the number of cases and deaths with the ratios of quintile-specific total fertility rate (TFR):

$$\mathrm{C_i} = [\mathrm{Ac_i} \times \mathrm{TC}_a + \mathrm{UAc_i} \times \mathrm{TC}_{ua}] \times \frac{\mathrm{TFR_i}}{\mathrm{TFR_{avg}}} \quad , \tag{1}$$

$$\mathrm{D_i} = [\mathrm{Ad_i} \times \mathrm{TD}_a + \mathrm{UAd_i} \times \mathrm{TD}_{ua}] \times \frac{\mathrm{TFR_i}}{\mathrm{TFR_{avg}}} \ , \tag{2}$$

where $\mathrm{TFR_i}$ and $\mathrm{TFR_{avg}}$ are the quintile-specific and national average of total fertility rate, respectively.

The distribution of cases with and without vaccines, and the distribution of deaths among the remaining cases not averted by vaccines, with and without treatment access, with TFR adjustment are presented in Table S4.1. Higher TFR in poorer quintiles leads to greater number of susceptible children and therefore larger proportions of cases and deaths in these quintiles. Table S4.2 shows the differences in AUC between scenarios S1 and S2 for both cases and deaths. For measles cases, the changes in AUC between the two scenarios are smaller under the TFR adjustment than the original analysis, suggesting that, while the MCV program still leads to greater unequal distribution of cases, the effect is attenuated with the TFR adjustment. This is because TFR adjustment increases the baseline AUC (AUC in S1), thus reducing the differences of AUC between S1 and S2. Changes in AUC are minimal for measles deaths. Similar results are found for PCV and RV.

Sensitivity analysis 2. *Replacing the flat distribution of the unattributable cases and deaths with a distribution comparable to the distribution of quintile-specific under-five mortality rates.*

Instead of assuming that unattributable cases and deaths ($\mathrm{UAc_i}$ and $\mathrm{UAd_i}$) follow a flat distribution, I replaced it with the ratios of under-five mortality rates from each quintile ($\mathrm{U5M_i}$) to check the impact on our findings:

$$\mathrm{UAc_i} = \mathrm{UAd_i} = \frac{\mathrm{U5M}_i}{\sum_{i=1}^{5} \mathrm{U5M}_i} \quad . \tag{3}$$

I found that the changes in the distribution and the AUC were small (less than 5%) (Tables S4.3 and S4.4).

Sensitivity analysis 3. *One-way sensitivity analysis of the relative risks of each risk and prognostic factor.*
To account for the uncertainty in the relative risk estimates, I conducted one-way sensitivity analyses for each risk and prognostic factor. Table S4.5 shows the ranges of the relative and prognostic risks provided from the literature. I estimated the changes in AUC between scenarios S1 and S2 with the upper and lower bounds of each risk and prognostic factor to identify results that are sensitive to the relative risk assumptions. I considered results that are 20% different from the original results and the absolute difference in the AUC between S1 and S2 to be greater than 10 units (4% of total AUC) to be sensitive to the assumptions. Only one set of results matched this definition: non-exclusive breastfeeding as a prognostic factor for pneumonia deaths in Ethiopia. The percentage difference compared to the original results was -20% to 24%, with the lower and upper bound of the relative risk, respectively. I conclude from this set of sensitivity analyses that the results are not sensitive to the assumptions of relative risks.

Table S4.3. Sensitivity analysis – distribution of cases and deaths with total fertility rate adjustment

Quintile: 1: poorest, 2: poorer, 3: middle, 4: richer, 5: richest.
N/A: estimates not available due to no vaccine introduction in 2016.
Cases S1: distribution of cases under the assumption of zero vaccine coverage.
Cases S2: distribution of remaining cases after current vaccine coverage rates.
Deaths S1: distribution of remaining cases not averted by vaccine programs, under the hypothetical scenario of people not having access to any treatment.
Deaths S2: distribution of deaths with current treatment utilization rates.
MCV: measles first dose, PCV: pneumococcal conjugate vaccine, RV: rotavirus vaccine.
TFR: total fertility rate.

			MCV				PCV				RV			
Country	Quintile	TFR	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2
	1	1.80	0.27	0.28	0.35	0.37	0.31	0.31	0.42	0.44	0.35	0.35	0.47	0.50
	2	1.80	0.22	0.19	0.19	0.20	0.21	0.21	0.19	0.20	0.22	0.21	0.18	0.19
	3	1.60	0.17	0.16	0.14	0.14	0.16	0.15	0.11	0.11	0.14	0.14	0.09	0.09
	4	1.80	0.20	0.21	0.19	0.18	0.24	0.23	0.22	0.20	0.23	0.22	0.21	0.18
Armenia	5	1.50	0.14	0.16	0.13	0.12	0.10	0.10	0.06	0.05	0.08	0.08	0.04	0.03
	1	3.10	0.33	0.40	0.46	0.47	0.30	0.30	0.34	0.36	0.32	N/A	N/A	N/A
	2	2.50	0.23	0.21	0.21	0.22	0.22	0.22	0.23	0.24	0.23	N/A	N/A	N/A
	3	2.20	0.19	0.17	0.16	0.17	0.19	0.19	0.19	0.20	0.20	N/A	N/A	N/A
	4	2.10	0.15	0.13	0.10	0.09	0.15	0.15	0.12	0.11	0.15	N/A	N/A	N/A
Bangladesh	5	1.90	0.13	0.09	0.07	0.05	0.14	0.14	0.12	0.09	0.13	N/A	N/A	N/A
	1	6.10	0.29	0.35	0.40	0.43	0.30	0.31	0.37	0.40	0.32	N/A	N/A	N/A
	2	5.40	0.21	0.22	0.21	0.21	0.21	0.21	0.19	0.19	0.21	N/A	N/A	N/A
	3	5.10	0.22	0.20	0.20	0.18	0.22	0.21	0.22	0.19	0.23	N/A	N/A	N/A
	4	4.60	0.16	0.13	0.11	0.11	0.15	0.15	0.11	0.11	0.14	N/A	N/A	N/A
Benin	5	3.90	0.13	0.09	0.07	0.07	0.13	0.13	0.10	0.10	0.12	N/A	N/A	N/A
	1	7.10	0.28	0.35	0.39	0.42	0.26	0.26	0.29	0.34	0.27	0.27	0.30	0.34
Burkina Faso	2	6.90	0.24	0.24	0.24	0.24	0.23	0.22	0.22	0.24	0.24	0.23	0.24	0.25

	3	6.70	0.22	0.20	0.19	0.17	0.23	0.22	0.22	0.19	0.23	0.23	0.23	0.22
	4	6.20	0.19	0.15	0.13	0.12	0.19	0.19	0.18	0.17	0.19	0.19	0.17	0.14
	5	3.70	0.10	0.07	0.05	0.05	0.11	0.10	0.08	0.07	0.09	0.09	0.06	0.05
	1	6.20	0.24	0.27	0.32	0.32	0.22	0.22	0.24	0.25	0.22	0.22	0.26	0.26
	2	6.80	0.22	0.22	0.21	0.22	0.21	0.21	0.20	0.21	0.21	0.21	0.20	0.20
	3	6.50	0.21	0.20	0.20	0.19	0.19	0.19	0.19	0.18	0.21	0.20	0.20	0.19
	4	6.80	0.20	0.19	0.17	0.18	0.19	0.19	0.18	0.18	0.20	0.20	0.18	0.20
Burundi	5	5.70	0.14	0.13	0.10	0.09	0.19	0.19	0.19	0.18	0.16	0.16	0.16	0.15
	1	3.80	0.32	0.43	0.47	0.47	0.28	0.29	0.32	0.32	0.32	N/A	N/A	N/A
	2	2.80	0.22	0.24	0.24	0.25	0.19	0.20	0.20	0.21	0.22	N/A	N/A	N/A
	3	2.80	0.19	0.16	0.14	0.14	0.18	0.18	0.17	0.15	0.18	N/A	N/A	N/A
	4	2.40	0.16	0.10	0.09	0.09	0.16	0.16	0.15	0.16	0.16	N/A	N/A	N/A
Cambodia	5	2.20	0.12	0.07	0.05	0.06	0.18	0.17	0.16	0.17	0.14	N/A	N/A	N/A
	1	7.00	0.40	0.51	0.62	0.65	0.37	0.36	0.49	0.55	0.47	0.44	0.56	0.59
	2	6.40	0.28	0.26	0.23	0.21	0.26	0.25	0.25	0.22	0.29	0.26	0.24	0.23
	3	5.60	0.19	0.13	0.09	0.08	0.20	0.19	0.15	0.13	0.19	0.16	0.12	0.11
	4	4.20	0.12	0.07	0.05	0.04	0.13	0.12	0.08	0.07	0.10	0.09	0.05	0.05
Cameroon	5	3.30	0.08	0.03	0.02	0.02	0.10	0.07	0.04	0.04	0.06	0.05	0.03	0.02
	1	7.00	0.21	0.22	0.22	0.23	0.20	N/A	N/A	N/A	0.21	N/A	N/A	N/A
	2	7.00	0.21	0.21	0.20	0.21	0.21	N/A	N/A	N/A	0.21	N/A	N/A	N/A
	3	6.80	0.23	0.23	0.25	0.25	0.24	N/A	N/A	N/A	0.24	N/A	N/A	N/A
	4	6.20	0.21	0.22	0.23	0.22	0.20	N/A	N/A	N/A	0.20	N/A	N/A	N/A
Chad	5	5.30	0.14	0.12	0.10	0.09	0.16	N/A	N/A	N/A	0.14	N/A	N/A	N/A
	1	6.70	0.38	0.47	0.54	0.53	0.37	N/A	N/A	N/A	0.39	N/A	N/A	N/A
	2	4.60	0.22	0.23	0.22	0.23	0.21	N/A	N/A	N/A	0.21	N/A	N/A	N/A
	3	4.20	0.18	0.12	0.10	0.11	0.19	N/A	N/A	N/A	0.19	N/A	N/A	N/A
	4	3.50	0.15	0.10	0.08	0.08	0.15	N/A	N/A	N/A	0.14	N/A	N/A	N/A
Comoros	5	3.40	0.11	0.09	0.06	0.06	0.12	N/A	N/A	N/A	0.12	N/A	N/A	N/A
	1	7.00	0.34	0.44	0.50	0.51	0.28	0.30	0.33	0.36	0.35	0.34	0.39	0.40
Congo	2	6.10	0.27	0.27	0.27	0.27	0.25	0.25	0.28	0.28	0.28	0.27	0.29	0.29

	3	4.90	0.19	0.14	0.12	0.13	0.18	0.18	0.16	0.17	0.18	0.17	0.15	0.16
	4	4.10	0.14	0.09	0.07	0.06	0.16	0.15	0.13	0.11	0.13	0.12	0.10	0.10
	5	3.80	0.11	0.06	0.04	0.03	0.14	0.13	0.10	0.08	0.10	0.09	0.07	0.05
	1	6.70	0.33	0.36	0.43	0.46	0.28	0.29	0.32	0.37	0.33	0.32	0.36	0.39
	2	6.00	0.24	0.26	0.25	0.24	0.23	0.23	0.23	0.24	0.25	0.24	0.24	0.22
	3	5.50	0.21	0.19	0.18	0.17	0.21	0.21	0.20	0.17	0.21	0.20	0.19	0.20
	4	4.30	0.15	0.13	0.10	0.09	0.16	0.15	0.14	0.13	0.15	0.14	0.12	0.12
Côte d'Ivoire	5	3.20	0.10	0.06	0.04	0.04	0.12	0.11	0.10	0.09	0.10	0.10	0.08	0.08
	1	7.60	0.28	0.33	0.36	0.37	0.25	0.26	0.28	0.29	0.27	N/A	N/A	N/A
	2	7.40	0.27	0.28	0.30	0.29	0.26	0.26	0.29	0.30	0.27	N/A	N/A	N/A
	3	7.10	0.24	0.21	0.21	0.20	0.22	0.22	0.22	0.21	0.24	N/A	N/A	N/A
	4	6.50	0.17	0.14	0.10	0.11	0.18	0.17	0.14	0.14	0.17	N/A	N/A	N/A
Democratic Republic of the Congo	5	4.90	0.08	0.05	0.03	0.03	0.11	0.10	0.06	0.06	0.09	N/A	N/A	N/A
	1	6.00	0.29	0.33	0.37	0.38	0.27	0.28	0.31	0.33	0.30	0.29	0.32	0.34
	2	5.70	0.27	0.27	0.29	0.29	0.28	0.28	0.33	0.33	0.30	0.29	0.33	0.35
	3	5.30	0.22	0.21	0.20	0.19	0.18	0.18	0.16	0.16	0.20	0.20	0.17	0.15
	4	5.00	0.18	0.16	0.13	0.12	0.18	0.16	0.13	0.13	0.17	0.16	0.13	0.12
Ethiopia	5	2.80	0.08	0.03	0.02	0.01	0.10	0.09	0.07	0.05	0.08	0.07	0.05	0.04
	1	6.70	0.24	0.20	0.20	0.20	0.21	0.21	0.18	0.18	0.21	0.21	0.18	0.18
	2	6.80	0.25	0.23	0.23	0.23	0.23	0.23	0.22	0.22	0.24	0.23	0.23	0.21
	3	6.20	0.25	0.23	0.26	0.26	0.26	0.26	0.31	0.30	0.26	0.26	0.31	0.31
	4	5.30	0.17	0.16	0.15	0.16	0.19	0.19	0.18	0.19	0.18	0.18	0.18	0.18
The Gambia	5	3.80	0.11	0.18	0.16	0.16	0.12	0.12	0.11	0.11	0.12	0.12	0.11	0.11
	1	6.30	0.36	0.38	0.44	0.42	0.30	0.30	0.34	0.33	0.36	0.35	0.39	0.34
	2	5.50	0.26	0.25	0.24	0.24	0.24	0.24	0.24	0.24	0.26	0.25	0.25	0.25
	3	3.90	0.15	0.14	0.11	0.12	0.15	0.15	0.12	0.13	0.15	0.14	0.12	0.15
	4	3.50	0.16	0.15	0.14	0.15	0.17	0.17	0.17	0.17	0.16	0.15	0.15	0.16
Ghana	5	2.80	0.11	0.08	0.06	0.06	0.13	0.13	0.12	0.12	0.11	0.10	0.10	0.10
	1	6.50	0.31	0.35	0.40	0.43	0.31	N/A	N/A	N/A	0.35	N/A	N/A	N/A
Guinea	2	5.50	0.24	0.21	0.22	0.22	0.21	N/A	N/A	N/A	0.23	N/A	N/A	N/A

	3	5.70	0.24	0.23	0.22	0.21	0.23	N/A	N/A	N/A	0.24	N/A	N/A	N/A
	4	4.80	0.17	0.15	0.12	0.11	0.17	N/A	N/A	N/A	0.16	N/A	N/A	N/A
	5	3.40	0.08	0.06	0.04	0.03	0.10	N/A	N/A	N/A	0.07	N/A	N/A	N/A
	1	5.70	0.32	0.32	0.34	0.36	0.30	0.30	0.30	0.33	0.36	0.34	0.37	0.38
	2	4.70	0.25	0.25	0.25	0.25	0.25	0.24	0.24	0.25	0.27	0.26	0.26	0.27
	3	3.80	0.20	0.19	0.18	0.18	0.19	0.19	0.18	0.18	0.19	0.18	0.16	0.15
	4	3.10	0.16	0.16	0.16	0.15	0.19	0.19	0.22	0.19	0.18	0.17	0.18	0.16
Haiti	5	1.90	0.08	0.08	0.07	0.06	0.08	0.08	0.06	0.05	0.06	0.05	0.04	0.03
	1	4.60	0.34	0.31	0.35	0.36	0.24	0.24	0.23	0.24	0.34	0.33	0.32	0.32
	2	3.30	0.22	0.22	0.21	0.21	0.21	0.22	0.21	0.23	0.22	0.21	0.21	0.21
	3	2.90	0.19	0.20	0.19	0.19	0.21	0.22	0.24	0.24	0.20	0.19	0.21	0.22
	4	2.40	0.15	0.16	0.15	0.15	0.17	0.17	0.17	0.17	0.14	0.14	0.14	0.13
Honduras	5	2.00	0.12	0.11	0.10	0.10	0.14	0.15	0.15	0.13	0.12	0.12	0.12	0.12
	1	3.20	0.30	0.33	0.38	0.41	0.27	N/A	N/A	N/A	0.30	N/A	N/A	N/A
	2	2.70	0.23	0.23	0.24	0.23	0.23	N/A	N/A	N/A	0.23	N/A	N/A	N/A
	3	2.50	0.18	0.15	0.14	0.13	0.15	N/A	N/A	N/A	0.17	N/A	N/A	N/A
	4	2.40	0.18	0.17	0.16	0.14	0.20	N/A	N/A	N/A	0.18	N/A	N/A	N/A
Indonesia	5	2.20	0.13	0.12	0.09	0.09	0.16	N/A	N/A	N/A	0.14	N/A	N/A	N/A
	1	6.40	0.39	0.44	0.51	0.51	0.37	0.36	0.42	0.43	0.41	0.39	0.47	0.45
	2	4.70	0.24	0.22	0.21	0.21	0.23	0.22	0.21	0.21	0.23	0.22	0.20	0.20
	3	3.80	0.19	0.16	0.15	0.15	0.21	0.20	0.20	0.20	0.19	0.18	0.18	0.19
	4	3.10	0.13	0.09	0.07	0.08	0.12	0.12	0.09	0.09	0.12	0.11	0.08	0.09
Kenya	5	2.80	0.10	0.08	0.06	0.05	0.11	0.11	0.08	0.07	0.10	0.10	0.07	0.07
	1	4.00	0.23	0.21	0.23	0.23	0.21	0.20	0.21	0.21	0.25	N/A	N/A	N/A
	2	4.10	0.21	0.19	0.19	0.20	0.24	0.23	0.24	0.26	0.21	N/A	N/A	N/A
	3	3.90	0.21	0.20	0.21	0.23	0.21	0.21	0.21	0.23	0.22	N/A	N/A	N/A
	4	4.00	0.21	0.25	0.24	0.23	0.22	0.22	0.21	0.20	0.20	N/A	N/A	N/A
Kyrgyz Republic	5	2.70	0.14	0.15	0.15	0.11	0.14	0.14	0.13	0.10	0.13	N/A	N/A	N/A
	1	5.00	0.36	0.37	0.42	0.41	0.33	0.32	0.37	0.38	0.41	N/A	N/A	N/A
Lesotho	2	3.90	0.26	0.29	0.30	0.29	0.24	0.23	0.25	0.23	0.27	N/A	N/A	N/A

	3	3.80	0.21	0.14	0.12	0.13	0.20	0.19	0.17	0.17	0.20	N/A	N/A	N/A
	4	2.70	0.14	0.13	0.10	0.11	0.15	0.14	0.12	0.12	0.12	N/A	N/A	N/A
	5	2.10	0.09	0.08	0.06	0.06	0.11	0.11	0.09	0.09	0.08	N/A	N/A	N/A
	1	6.60	0.32	0.34	0.37	0.39	0.29	0.30	0.33	0.34	0.32	0.31	0.34	0.36
	2	5.90	0.27	0.25	0.27	0.26	0.23	0.23	0.23	0.22	0.26	0.25	0.25	0.25
	3	5.20	0.22	0.21	0.20	0.19	0.21	0.21	0.21	0.19	0.22	0.21	0.21	0.19
	4	3.90	0.14	0.12	0.10	0.11	0.15	0.15	0.14	0.15	0.14	0.14	0.12	0.13
Liberia	5	2.80	0.09	0.07	0.06	0.06	0.11	0.11	0.10	0.10	0.10	0.09	0.08	0.08
	1	6.80	0.30	0.30	0.36	0.37	0.31	0.30	0.37	0.40	0.34	0.32	0.40	0.39
	2	6.80	0.26	0.25	0.26	0.26	0.27	0.26	0.26	0.27	0.27	0.25	0.26	0.26
	3	6.30	0.23	0.22	0.21	0.21	0.23	0.22	0.21	0.19	0.24	0.22	0.21	0.22
	4	5.30	0.16	0.14	0.12	0.11	0.14	0.13	0.09	0.09	0.13	0.13	0.09	0.08
Malawi	5	3.70	0.09	0.08	0.06	0.06	0.10	0.09	0.06	0.05	0.07	0.07	0.04	0.05
	1	6.70	0.26	0.32	0.35	0.37	0.25	0.26	0.29	0.32	0.27	0.27	0.30	0.34
	2	6.80	0.26	0.27	0.29	0.29	0.25	0.25	0.28	0.29	0.26	0.26	0.28	0.27
	3	6.60	0.23	0.23	0.23	0.22	0.23	0.22	0.23	0.22	0.23	0.23	0.23	0.24
	4	6.10	0.16	0.12	0.09	0.08	0.17	0.16	0.12	0.10	0.15	0.14	0.11	0.09
Mali	5	4.70	0.11	0.06	0.04	0.04	0.13	0.11	0.09	0.07	0.11	0.10	0.07	0.06
	1	7.20	0.34	0.37	0.46	0.47	0.32	0.32	0.41	0.42	0.37	0.35	0.44	0.46
	2	7.20	0.27	0.29	0.28	0.29	0.28	0.27	0.27	0.29	0.27	0.25	0.25	0.27
	3	6.30	0.22	0.21	0.18	0.16	0.22	0.21	0.19	0.17	0.21	0.20	0.18	0.16
	4	5.60	0.14	0.09	0.06	0.05	0.14	0.13	0.09	0.08	0.14	0.13	0.08	0.07
Mozambique	5	3.70	0.08	0.04	0.02	0.02	0.09	0.08	0.05	0.04	0.08	0.07	0.04	0.03
	1	4.10	0.38	0.37	0.42	0.43	0.30	0.31	0.32	0.35	0.35	N/A	N/A	N/A
	2	3.10	0.25	0.25	0.24	0.24	0.21	0.21	0.21	0.21	0.24	N/A	N/A	N/A
	3	2.70	0.21	0.22	0.21	0.20	0.21	0.21	0.22	0.22	0.22	N/A	N/A	N/A
	4	2.10	0.15	0.12	0.10	0.09	0.16	0.16	0.16	0.15	0.15	N/A	N/A	N/A
Nepal	5	1.50	0.07	0.05	0.03	0.03	0.11	0.11	0.09	0.09	0.08	N/A	N/A	N/A
	1	8.40	0.25	0.28	0.33	0.37	0.25	0.26	0.31	0.36	0.26	0.27	0.32	0.37
Niger	2	8.30	0.20	0.21	0.20	0.20	0.19	0.19	0.17	0.19	0.19	0.19	0.17	0.15

	3	9.20	0.24	0.26	0.27	0.25	0.25	0.25	0.27	0.24	0.25	0.25	0.27	0.25
	4	8.90	0.19	0.16	0.13	0.13	0.17	0.17	0.13	0.13	0.17	0.16	0.13	0.13
	5	7.10	0.14	0.09	0.07	0.06	0.15	0.13	0.11	0.07	0.14	0.13	0.11	0.10
	1	7.00	0.32	0.41	0.46	0.48	0.29	0.32	0.36	0.38	0.30	N/A	N/A	N/A
	2	6.70	0.28	0.31	0.31	0.31	0.27	0.28	0.30	0.31	0.27	N/A	N/A	N/A
	3	5.70	0.20	0.16	0.14	0.13	0.20	0.18	0.17	0.16	0.20	N/A	N/A	N/A
	4	4.90	0.15	0.09	0.07	0.06	0.16	0.13	0.11	0.11	0.16	N/A	N/A	N/A
Nigeria	5	3.90	0.10	0.03	0.02	0.02	0.11	0.09	0.06	0.04	0.10	N/A	N/A	N/A
	1	5.20	0.39	0.49	0.60	0.62	0.36	0.38	0.48	0.50	0.38	N/A	N/A	N/A
	2	4.40	0.24	0.21	0.19	0.19	0.23	0.22	0.20	0.21	0.24	N/A	N/A	N/A
	3	3.80	0.18	0.15	0.12	0.12	0.19	0.18	0.16	0.16	0.20	N/A	N/A	N/A
	4	3.40	0.14	0.09	0.06	0.05	0.14	0.13	0.09	0.07	0.13	N/A	N/A	N/A
Pakistan	5	2.70	0.10	0.05	0.03	0.03	0.12	0.10	0.08	0.06	0.10	N/A	N/A	N/A
	1	5.40	0.28	0.28	0.32	0.35	0.27	0.27	0.31	0.35	0.29	0.28	0.32	0.39
	2	5.20	0.25	0.27	0.29	0.28	0.25	0.25	0.27	0.27	0.26	0.26	0.28	0.26
	3	4.50	0.19	0.19	0.17	0.16	0.12	0.12	0.09	0.09	0.15	0.15	0.11	0.10
	4	4.40	0.18	0.16	0.14	0.14	0.19	0.19	0.17	0.19	0.18	0.18	0.16	0.15
Rwanda	5	3.40	0.12	0.10	0.08	0.07	0.17	0.17	0.16	0.11	0.14	0.13	0.13	0.11
	1	6.70	0.29	0.30	0.35	0.35	0.25	0.25	0.28	0.27	0.27	0.27	0.29	0.30
	2	6.80	0.25	0.25	0.25	0.25	0.23	0.23	0.23	0.24	0.24	0.23	0.23	0.21
	3	6.20	0.22	0.21	0.20	0.20	0.22	0.22	0.23	0.22	0.22	0.22	0.22	0.22
	4	5.30	0.17	0.15	0.13	0.13	0.18	0.18	0.16	0.15	0.17	0.17	0.16	0.18
Senegal	5	3.80	0.10	0.09	0.07	0.07	0.12	0.12	0.10	0.11	0.11	0.11	0.10	0.08
	1	6.10	0.24	0.22	0.21	0.22	0.23	0.23	0.22	0.23	0.24	0.24	0.24	0.24
	2	5.80	0.27	0.27	0.31	0.32	0.26	0.26	0.29	0.29	0.27	0.27	0.30	0.36
	3	5.50	0.23	0.24	0.24	0.22	0.22	0.22	0.22	0.21	0.23	0.22	0.22	0.17
	4	4.70	0.18	0.18	0.17	0.16	0.18	0.18	0.17	0.17	0.17	0.17	0.15	0.15
Sierra Leone	5	3.00	0.10	0.09	0.08	0.07	0.12	0.12	0.11	0.10	0.10	0.10	0.09	0.08
	1	4.10	0.25	0.27	0.31	0.32	0.24	N/A	N/A	N/A	0.25	0.25	0.28	0.31
Tajikistan	2	4.10	0.22	0.19	0.19	0.20	0.19	N/A	N/A	N/A	0.21	0.21	0.19	0.21

	3	3.90	0.19	0.19	0.17	0.15	0.19	N/A	N/A	N/A	0.18	0.18	0.16	0.12
	4	3.50	0.19	0.18	0.18	0.17	0.20	N/A	N/A	N/A	0.20	0.20	0.22	0.20
	5	3.20	0.16	0.17	0.16	0.16	0.17	N/A	N/A	N/A	0.16	0.16	0.15	0.15
	1	7.00	0.31	0.33	0.39	0.39	0.27	0.27	0.31	0.32	0.32	0.31	0.35	0.35
	2	6.80	0.26	0.25	0.25	0.24	0.22	0.23	0.21	0.21	0.23	0.23	0.21	0.20
	3	6.10	0.22	0.23	0.22	0.23	0.22	0.22	0.22	0.23	0.22	0.22	0.21	0.24
	4	4.70	0.15	0.11	0.09	0.09	0.16	0.16	0.14	0.14	0.15	0.14	0.13	0.13
Tanzania	5	3.20	0.10	0.07	0.06	0.05	0.12	0.12	0.12	0.10	0.10	0.10	0.10	0.08
	1	7.30	0.29	0.37	0.40	0.42	0.28	N/A	N/A	N/A	0.30	N/A	N/A	N/A
	2	6.00	0.22	0.23	0.23	0.23	0.20	N/A	N/A	N/A	0.21	N/A	N/A	N/A
	3	6.10	0.22	0.19	0.19	0.18	0.23	N/A	N/A	N/A	0.23	N/A	N/A	N/A
	4	5.30	0.17	0.12	0.10	0.11	0.17	N/A	N/A	N/A	0.17	N/A	N/A	N/A
Timor-Leste	5	4.20	0.12	0.09	0.07	0.06	0.13	N/A	N/A	N/A	0.12	N/A	N/A	N/A
	1	6.30	0.29	0.26	0.28	0.27	0.28	0.27	0.30	0.31	0.33	0.31	0.34	0.31
	2	5.80	0.27	0.30	0.32	0.32	0.25	0.25	0.26	0.24	0.27	0.26	0.27	0.29
	3	5.40	0.24	0.27	0.27	0.28	0.24	0.23	0.25	0.26	0.25	0.24	0.24	0.26
	4	3.90	0.15	0.12	0.10	0.10	0.16	0.15	0.14	0.14	0.14	0.13	0.11	0.10
Togo	5	3.50	0.09	0.06	0.04	0.03	0.10	0.10	0.06	0.04	0.07	0.06	0.03	0.03
	1	7.90	0.26	0.26	0.27	0.27	0.23	0.23	0.22	0.22	0.27	0.26	0.26	0.26
	2	7.10	0.24	0.25	0.26	0.26	0.24	0.24	0.27	0.27	0.26	0.25	0.27	0.27
	3	6.90	0.23	0.23	0.24	0.24	0.21	0.21	0.21	0.21	0.21	0.21	0.20	0.19
	4	6.10	0.19	0.17	0.17	0.17	0.20	0.20	0.21	0.21	0.20	0.19	0.19	0.19
Uganda	5	4.00	0.10	0.08	0.06	0.06	0.12	0.12	0.10	0.09	0.09	0.09	0.07	0.09
	1	6.10	0.37	0.43	0.52	0.52	0.34	0.35	0.42	0.43	0.37	0.36	0.44	0.45
	2	5.30	0.26	0.26	0.25	0.25	0.25	0.24	0.24	0.24	0.26	0.24	0.24	0.24
	3	4.50	0.19	0.16	0.13	0.13	0.18	0.17	0.14	0.14	0.17	0.17	0.14	0.14
	4	3.80	0.14	0.10	0.07	0.07	0.15	0.14	0.12	0.12	0.15	0.14	0.11	0.11
Yemen	5	2.90	0.09	0.05	0.03	0.03	0.11	0.10	0.08	0.07	0.10	0.09	0.07	0.06
	1	7.10	0.32	0.34	0.40	0.41	0.30	0.30	0.35	0.36	0.32	0.32	0.37	0.39
Zambia	2	7.00	0.25	0.27	0.26	0.26	0.24	0.24	0.22	0.23	0.25	0.24	0.23	0.22

	3	6.00	0.21	0.20	0.18	0.18	0.20	0.20	0.18	0.19	0.20	0.20	0.18	0.17
	4	4.20	0.15	0.12	0.12	0.11	0.16	0.15	0.16	0.15	0.16	0.15	0.15	0.14
	5	3.00	0.09	0.06	0.05	0.05	0.11	0.10	0.09	0.08	0.09	0.09	0.08	0.08
	1	5.30	0.29	0.28	0.31	0.30	0.29	0.29	0.32	0.31	0.33	0.31	0.36	0.35
	2	5.10	0.26	0.29	0.31	0.31	0.27	0.26	0.28	0.29	0.28	0.27	0.28	0.29
	3	4.40	0.21	0.24	0.23	0.23	0.20	0.19	0.17	0.16	0.19	0.18	0.16	0.17
	4	3.80	0.17	0.12	0.11	0.11	0.19	0.18	0.18	0.18	0.18	0.17	0.16	0.15
Zimbabwe	5	2.60	0.10	0.07	0.05	0.05	0.09	0.08	0.06	0.06	0.07	0.07	0.04	0.04

Table S4.4. Sensitivity analysis – changes in the area under the curve of the distribution of cases and deaths with total fertility rate adjustment

Δ AUC: changes in the area under the curve.
Difference in Δ AUC from original results: calculated as (Δ AUC from s1 to s2 under TFR adjustment) - (Δ AUC from s1 to s2 in the original analysis).
N/A: estimates not available due to no vaccine introduction in 2016.
Cases S1: distribution of cases under the assumption of zero vaccine coverage.
Cases S2: distribution of remaining cases after current vaccine coverage rates.
Deaths S1: distribution of remaining cases not averted by vaccine programs, under the hypothetical scenario of people not having access to any treatment.
Deaths S2: distribution of deaths with current treatment utilization rates.
MCV: measles first dose, PCV: pneumococcal conjugate vaccine, RV: rotavirus vaccine.

	MCV				PCV				RV			
	Cases: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Deaths: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Cases: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Deaths: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Cases: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Deaths: Δ AUC from s1 to s2	Difference in Δ AUC from original results
Armenia	-10	-2	9	0	-4	-5	9	0	-7	-8	12	0
Bangladesh	16	-8	7	-1	-3	-5	13	-1	N/A	N/A	N/A	N/A
Benin	19	-7	6	0	-2	-6	7	1	N/A	N/A	N/A	N/A
Burkina Faso	16	-9	10	-1	-3	-4	16	-2	-8	-9	15	-2
Burundi	9	-1	1	0	1	1	3	0	0	0	1	-1
Cambodia	33	-9	-2	0	4	0	1	0	N/A	N/A	N/A	N/A
Cameroon	16	-33	6	-1	-11	-20	11	-1	-35	-39	7	-2
Chad	5	-2	6	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Comoros	17	-13	-1	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Congo	24	-17	5	-2	2	-3	13	-2	-13	-16	6	-2
Côte d'Ivoire	9	-16	7	-1	3	-3	14	0	-9	-11	5	0
Democratic Republic of the Congo	10	-14	1	0	0	-6	3	0	N/A	N/A	N/A	N/A

Ethiopia	11	-22	5	-1	1	-6	10	-4	-11	-15	10	-4
The Gambia	-26	2	-2	0	-2	-1	-3	0	-2	-2	-3	0
Ghana	-3	-14	-6	0	0	0	-3	0	-12	-12	-11	-1
Guinea	3	-15	10	-2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Haiti	-8	-7	8	-2	-2	-2	13	-1	-17	-19	8	-3
Honduras	-11	-8	2	0	9	9	6	0	-6	-6	0	0
Indonesia	7	-5	5	1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Kenya	4	-17	0	0	-11	-12	3	-1	-19	-19	-6	0
Kyrgyz Republic	-12	0	11	-2	-4	-1	12	-3	N/A	N/A	N/A	N/A
Lesotho	-5	-15	-2	0	-6	-6	2	0	N/A	N/A	N/A	N/A
Liberia	-3	-15	1	1	1	-2	-2	2	-9	-10	4	0
Malawi	-3	-12	3	0	-11	-12	8	-1	-18	-18	-3	1
Mali	18	-10	6	-1	1	-5	12	-2	-5	-7	9	-1
Mozambique	6	-24	4	-1	-11	-15	7	-2	-17	-19	10	-2
Nepal	-8	-24	3	0	2	0	6	0	N/A	N/A	N/A	N/A
Niger	19	-4	9	-1	4	-2	20	-2	2	-2	11	-1
Nigeria	31	-21	5	-1	4	-10	9	-2	N/A	N/A	N/A	N/A
Pakistan	19	-22	5	-2	-2	-12	10	-3	N/A	N/A	N/A	N/A
Rwanda	4	-7	8	-1	0	0	15	-3	-5	-5	15	-1
Senegal	-1	-10	-1	0	-1	-2	-3	2	-4	-5	1	-1
Sierra Leone	-9	-7	3	0	-2	-1	3	0	-5	-5	9	-1
Tajikistan	3	0	5	0	N/A	N/A	N/A	N/A	-1	-1	10	0
Tanzania	3	-14	1	-1	3	2	6	-3	-6	-7	3	-4
Timor-Leste	23	-6	5	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Togo	-3	-17	1	-1	-7	-8	4	-2	-18	-18	-2	-2
Uganda	1	-9	-1	0	-1	-1	1	-1	-8	-8	-4	2
Yemen	10	-23	2	-1	-4	-10	3	-1	-12	-15	5	-1
Zambia	7	-14	3	-1	1	-2	7	-3	-6	-7	3	2
Zimbabwe	6	-13	-1	0	-8	-10	-2	1	-16	-17	-1	-1

Table S4.5. Sensitivity analysis – distribution of cases and deaths with under-five mortality rate adjustment

Quintile: 1: poorest, 2: poorer, 3: middle, 4: richer, 5: richest.
U5MR: under-five mortality rate.
N/A: estimates not available due to no vaccine introduction in 2016.
Cases S1: distribution of cases under the assumption of zero vaccine coverage.
Cases S2: distribution of remaining cases after current vaccine coverage rates.
Deaths S1: distribution of remaining cases not averted by vaccine programs, under the hypothetical scenario of people not having access to any treatment.
Deaths S2: distribution of deaths with current treatment utilization rates.
MCV: measles first dose, PCV: pneumococcal conjugate vaccine, RV: rotavirus vaccine.

			MCV				PCV				RV			
Country	Quintile	U5MR	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2	Cases S1	Cases S2	Deaths S1	Deaths S2
	1	25	0.28	0.29	0.36	0.38	0.30	0.31	0.42	0.44	0.34	0.47	0.50	0.34
	2	29	0.25	0.22	0.22	0.23	0.22	0.22	0.20	0.21	0.22	0.19	0.20	0.22
	3	17	0.16	0.15	0.13	0.13	0.15	0.15	0.11	0.11	0.14	0.10	0.09	0.14
	4	14	0.15	0.16	0.15	0.13	0.21	0.21	0.20	0.18	0.21	0.20	0.17	0.21
Armenia	5	21	0.16	0.18	0.15	0.13	0.12	0.11	0.07	0.06	0.09	0.05	0.04	0.09
	1	64	0.26	0.33	0.39	0.40	0.23	0.23	0.27	0.29	N/A	N/A	N/A	N/A
	2	64	0.23	0.22	0.22	0.23	0.21	0.22	0.23	0.24	N/A	N/A	N/A	N/A
	3	49	0.20	0.19	0.19	0.19	0.21	0.21	0.21	0.22	N/A	N/A	N/A	N/A
	4	48	0.17	0.15	0.12	0.11	0.17	0.17	0.14	0.13	N/A	N/A	N/A	N/A
Bangladesh	5	37	0.15	0.11	0.08	0.06	0.18	0.17	0.15	0.11	N/A	N/A	N/A	N/A
	1	88	0.25	0.31	0.36	0.38	0.25	0.26	0.32	0.35	N/A	N/A	N/A	N/A
	2	90	0.21	0.22	0.21	0.21	0.20	0.20	0.18	0.19	N/A	N/A	N/A	N/A
	3	80	0.22	0.21	0.21	0.20	0.22	0.22	0.23	0.20	N/A	N/A	N/A	N/A
	4	65	0.17	0.15	0.13	0.12	0.17	0.16	0.13	0.13	N/A	N/A	N/A	N/A
Benin	5	44	0.15	0.11	0.09	0.09	0.17	0.16	0.13	0.13	N/A	N/A	N/A	N/A
Burkina Faso	1	175	0.25	0.32	0.37	0.40	0.23	0.23	0.26	0.31	0.24	0.27	0.31	0.24

	2	173	0.22	0.23	0.23	0.24	0.21	0.20	0.20	0.23	0.21	0.22	0.24	0.21
	3	144	0.21	0.19	0.18	0.17	0.21	0.21	0.21	0.18	0.21	0.22	0.22	0.21
	4	131	0.18	0.15	0.13	0.12	0.19	0.19	0.18	0.17	0.19	0.18	0.14	0.19
	5	97	0.15	0.12	0.09	0.07	0.17	0.17	0.14	0.11	0.14	0.11	0.09	0.14
	1	152	0.25	0.29	0.34	0.34	0.23	0.23	0.25	0.26	0.23	0.27	0.27	0.23
	2	137	0.21	0.21	0.21	0.21	0.20	0.20	0.19	0.20	0.20	0.19	0.19	0.20
	3	139	0.21	0.20	0.20	0.20	0.19	0.19	0.19	0.18	0.20	0.20	0.18	0.20
	4	121	0.19	0.17	0.16	0.16	0.18	0.18	0.16	0.17	0.19	0.17	0.19	0.19
Burundi	5	80	0.14	0.13	0.09	0.09	0.21	0.21	0.20	0.20	0.18	0.18	0.16	0.18
	1	76	0.27	0.38	0.42	0.41	0.22	0.23	0.25	0.25	N/A	N/A	N/A	N/A
	2	56	0.23	0.26	0.27	0.28	0.20	0.20	0.20	0.21	N/A	N/A	N/A	N/A
	3	41	0.19	0.17	0.15	0.14	0.18	0.18	0.17	0.15	N/A	N/A	N/A	N/A
	4	33	0.18	0.11	0.10	0.10	0.19	0.18	0.18	0.18	N/A	N/A	N/A	N/A
Cambodia	5	19	0.13	0.08	0.06	0.06	0.21	0.21	0.20	0.20	N/A	N/A	N/A	N/A
	1	184	0.33	0.47	0.58	0.62	0.29	0.30	0.43	0.49	0.38	0.51	0.54	0.38
	2	144	0.24	0.25	0.23	0.22	0.22	0.23	0.23	0.21	0.24	0.24	0.23	0.24
	3	120	0.18	0.13	0.10	0.09	0.19	0.19	0.16	0.14	0.17	0.13	0.12	0.17
	4	90	0.14	0.09	0.06	0.05	0.16	0.16	0.11	0.10	0.12	0.08	0.07	0.12
Cameroon	5	72	0.11	0.05	0.03	0.02	0.14	0.12	0.07	0.06	0.09	0.05	0.04	0.09
	1	161	0.20	0.21	0.20	0.22	0.18	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2	164	0.20	0.20	0.19	0.20	0.19	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	3	142	0.22	0.22	0.24	0.24	0.22	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	4	133	0.21	0.23	0.24	0.24	0.20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Chad	5	138	0.17	0.14	0.12	0.11	0.19	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	1	52	0.26	0.35	0.42	0.41	0.25	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	2	54	0.22	0.25	0.25	0.26	0.21	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	3	50	0.19	0.14	0.13	0.13	0.20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
	4	49	0.19	0.14	0.12	0.11	0.19	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Comoros	5	40	0.14	0.12	0.09	0.09	0.16	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Congo	1	89	0.26	0.37	0.43	0.44	0.21	0.23	0.26	0.29	0.27	0.32	0.33	0.27

	2	98	0.24	0.26	0.27	0.27	0.22	0.23	0.25	0.26	0.24	0.27	0.27	0.24
	3	81	0.20	0.16	0.15	0.15	0.19	0.19	0.18	0.20	0.19	0.18	0.19	0.19
	4	74	0.18	0.12	0.10	0.09	0.20	0.19	0.17	0.15	0.16	0.14	0.14	0.16
	5	54	0.13	0.08	0.05	0.04	0.18	0.17	0.14	0.11	0.13	0.10	0.07	0.13
	1	123	0.26	0.30	0.37	0.40	0.22	0.23	0.25	0.30	0.26	0.30	0.32	0.26
	2	129	0.22	0.24	0.24	0.24	0.20	0.21	0.21	0.22	0.21	0.22	0.20	0.21
	3	124	0.20	0.20	0.19	0.18	0.20	0.20	0.20	0.17	0.20	0.19	0.20	0.20
	4	108	0.18	0.16	0.14	0.12	0.19	0.19	0.18	0.16	0.18	0.16	0.15	0.18
Côte d'Ivoire	5	82	0.15	0.09	0.07	0.07	0.19	0.18	0.17	0.16	0.16	0.13	0.13	0.16
	1	117	0.25	0.31	0.34	0.35	0.22	0.23	0.26	0.27	0.24	N/A	N/A	N/A
	2	119	0.25	0.27	0.29	0.29	0.23	0.24	0.28	0.28	0.25	N/A	N/A	N/A
	3	122	0.23	0.21	0.21	0.20	0.21	0.21	0.22	0.21	0.22	N/A	N/A	N/A
Democratic Republic of the Congo	4	116	0.17	0.15	0.12	0.12	0.18	0.18	0.15	0.15	0.17	N/A	N/A	N/A
	5	76	0.10	0.06	0.03	0.03	0.15	0.14	0.09	0.09	0.11	N/A	N/A	N/A
	1	137	0.25	0.31	0.35	0.36	0.23	0.24	0.27	0.30	0.25	0.28	0.31	0.25
	2	121	0.24	0.26	0.28	0.28	0.24	0.25	0.31	0.32	0.26	0.31	0.33	0.26
	3	96	0.20	0.21	0.20	0.20	0.17	0.17	0.15	0.16	0.19	0.17	0.16	0.19
	4	100	0.17	0.17	0.14	0.13	0.18	0.17	0.14	0.13	0.17	0.14	0.13	0.17
Ethiopia	5	86	0.13	0.05	0.03	0.02	0.18	0.17	0.13	0.09	0.13	0.10	0.07	0.13
	1	70	0.21	0.18	0.18	0.18	0.18	0.18	0.16	0.16	0.18	0.16	0.16	0.18
	2	68	0.21	0.20	0.20	0.20	0.20	0.20	0.19	0.19	0.20	0.19	0.18	0.20
	3	70	0.24	0.22	0.25	0.25	0.24	0.24	0.29	0.28	0.25	0.29	0.30	0.25
	4	60	0.19	0.17	0.16	0.17	0.20	0.20	0.19	0.21	0.19	0.19	0.20	0.19
The Gambia	5	34	0.15	0.24	0.20	0.21	0.18	0.18	0.16	0.16	0.18	0.16	0.17	0.18
	1	92	0.27	0.30	0.36	0.34	0.22	0.22	0.25	0.24	0.26	0.29	0.25	0.26
	2	73	0.22	0.21	0.21	0.21	0.20	0.20	0.20	0.20	0.21	0.21	0.21	0.21
	3	61	0.16	0.16	0.13	0.14	0.17	0.17	0.14	0.14	0.16	0.14	0.17	0.16
	4	55	0.19	0.19	0.19	0.20	0.21	0.21	0.21	0.22	0.20	0.20	0.21	0.20
Ghana	5	64	0.16	0.13	0.11	0.11	0.21	0.21	0.20	0.20	0.17	0.16	0.16	0.17
Guinea	1	173	0.26	0.32	0.36	0.40	0.25	N/A	N/A	N/A	0.29	N/A	N/A	N/A

	2	141	0.23	0.22	0.23	0.23	0.20	N/A	N/A	N/A	0.21	N/A	N/A	N/A
	3	145	0.22	0.22	0.22	0.22	0.21	N/A	N/A	N/A	0.22	N/A	N/A	N/A
	4	109	0.18	0.16	0.14	0.12	0.19	N/A	N/A	N/A	0.17	N/A	N/A	N/A
	5	68	0.10	0.08	0.04	0.03	0.15	N/A	N/A	N/A	0.11	N/A	N/A	N/A
	1	104	0.24	0.24	0.26	0.28	0.20	0.20	0.21	0.24	0.25	0.27	0.29	0.25
	2	88	0.20	0.21	0.21	0.22	0.20	0.20	0.20	0.22	0.22	0.23	0.25	0.22
	3	96	0.21	0.20	0.20	0.20	0.19	0.19	0.19	0.19	0.19	0.18	0.17	0.19
	4	98	0.21	0.22	0.22	0.20	0.24	0.24	0.28	0.25	0.22	0.25	0.23	0.22
Haiti	5	62	0.13	0.14	0.12	0.10	0.16	0.16	0.12	0.10	0.11	0.08	0.06	0.11
	1	39	0.28	0.26	0.29	0.29	0.17	0.17	0.16	0.17	0.24	0.22	0.22	0.24
	2	27	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.20	0.20	0.20	0.19	0.20
	3	29	0.20	0.21	0.21	0.21	0.22	0.22	0.24	0.24	0.21	0.22	0.23	0.21
	4	28	0.19	0.21	0.19	0.19	0.21	0.21	0.21	0.21	0.18	0.18	0.17	0.18
Honduras	5	20	0.14	0.13	0.12	0.12	0.20	0.20	0.20	0.18	0.18	0.18	0.18	0.18
	1	70	0.28	0.32	0.36	0.39	0.24	N/A	N/A	N/A	0.25	N/A	N/A	N/A
	2	43	0.22	0.23	0.24	0.23	0.22	N/A	N/A	N/A	0.22	N/A	N/A	N/A
	3	39	0.19	0.16	0.14	0.14	0.16	N/A	N/A	N/A	0.17	N/A	N/A	N/A
	4	34	0.18	0.18	0.17	0.15	0.21	N/A	N/A	N/A	0.19	N/A	N/A	N/A
Indonesia	5	23	0.13	0.12	0.09	0.09	0.18	N/A	N/A	N/A	0.16	N/A	N/A	N/A
	1	57	0.25	0.32	0.38	0.38	0.24	0.25	0.29	0.31	0.27	0.34	0.32	0.27
	2	63	0.22	0.22	0.22	0.22	0.21	0.21	0.21	0.21	0.21	0.20	0.20	0.21
	3	54	0.20	0.20	0.19	0.19	0.22	0.22	0.24	0.24	0.21	0.22	0.23	0.21
	4	58	0.18	0.14	0.12	0.12	0.17	0.16	0.13	0.14	0.16	0.13	0.13	0.16
Kenya	5	47	0.14	0.12	0.09	0.09	0.16	0.16	0.12	0.11	0.15	0.11	0.12	0.15
	1	36	0.22	0.20	0.22	0.23	0.20	0.19	0.20	0.21	0.23	N/A	N/A	N/A
	2	34	0.20	0.18	0.17	0.19	0.22	0.22	0.22	0.24	0.19	N/A	N/A	N/A
	3	40	0.22	0.22	0.22	0.24	0.21	0.21	0.21	0.24	0.21	N/A	N/A	N/A
	4	27	0.18	0.21	0.20	0.19	0.19	0.20	0.19	0.18	0.18	N/A	N/A	N/A
Kyrgyz Republic	5	28	0.18	0.19	0.19	0.14	0.18	0.19	0.18	0.13	0.17	N/A	N/A	N/A
Lesotho	1	77	0.24	0.26	0.32	0.31	0.22	0.23	0.27	0.28	0.29	N/A	N/A	N/A

	2	87	0.23	0.27	0.29	0.29	0.21	0.21	0.23	0.22	0.24	N/A	N/A	N/A
	3	105	0.20	0.15	0.13	0.14	0.19	0.19	0.17	0.17	0.18	N/A	N/A	N/A
	4	120	0.20	0.19	0.17	0.17	0.20	0.20	0.18	0.18	0.16	N/A	N/A	N/A
	5	70	0.13	0.13	0.09	0.09	0.18	0.18	0.15	0.15	0.13	N/A	N/A	N/A
	1	130	0.24	0.27	0.31	0.32	0.22	0.23	0.26	0.26	0.24	0.27	0.29	0.24
	2	112	0.22	0.22	0.24	0.24	0.19	0.19	0.20	0.18	0.21	0.21	0.22	0.21
	3	105	0.20	0.21	0.20	0.19	0.20	0.20	0.20	0.18	0.20	0.21	0.18	0.20
	4	112	0.18	0.16	0.14	0.15	0.19	0.19	0.18	0.19	0.18	0.16	0.17	0.18
Liberia	5	99	0.15	0.13	0.10	0.10	0.20	0.19	0.17	0.19	0.16	0.15	0.14	0.16
	1	133	0.25	0.27	0.33	0.34	0.26	0.27	0.34	0.37	0.29	0.37	0.36	0.29
	2	140	0.23	0.23	0.24	0.24	0.23	0.23	0.24	0.25	0.23	0.24	0.24	0.23
	3	129	0.21	0.22	0.21	0.20	0.21	0.21	0.21	0.19	0.22	0.21	0.22	0.22
	4	126	0.18	0.16	0.13	0.13	0.15	0.15	0.11	0.10	0.15	0.10	0.10	0.15
Malawi	5	105	0.13	0.12	0.09	0.08	0.15	0.15	0.09	0.09	0.12	0.07	0.08	0.12
	1	112	0.24	0.31	0.34	0.36	0.23	0.25	0.28	0.31	0.25	0.29	0.33	0.25
	2	118	0.24	0.26	0.28	0.28	0.23	0.23	0.26	0.27	0.24	0.27	0.26	0.24
	3	130	0.22	0.23	0.23	0.23	0.21	0.21	0.22	0.22	0.22	0.23	0.24	0.22
	4	91	0.16	0.13	0.10	0.08	0.17	0.16	0.12	0.11	0.15	0.11	0.10	0.15
Mali	5	61	0.13	0.08	0.05	0.04	0.16	0.15	0.11	0.09	0.14	0.10	0.08	0.14
	1	129	0.30	0.35	0.44	0.45	0.27	0.28	0.37	0.39	0.32	0.41	0.43	0.32
	2	105	0.23	0.27	0.26	0.28	0.23	0.23	0.24	0.27	0.22	0.23	0.25	0.22
	3	114	0.21	0.22	0.19	0.18	0.21	0.21	0.20	0.18	0.20	0.19	0.17	0.20
	4	95	0.15	0.10	0.07	0.06	0.15	0.15	0.10	0.10	0.14	0.10	0.08	0.14
Mozambique	5	91	0.12	0.07	0.04	0.03	0.14	0.13	0.08	0.06	0.12	0.07	0.06	0.12
	1	75	0.26	0.28	0.32	0.34	0.20	0.21	0.22	0.24	0.23	N/A	N/A	N/A
	2	66	0.22	0.24	0.24	0.24	0.19	0.19	0.18	0.19	0.21	N/A	N/A	N/A
	3	64	0.22	0.24	0.24	0.23	0.21	0.21	0.23	0.22	0.22	N/A	N/A	N/A
	4	59	0.19	0.16	0.14	0.14	0.21	0.20	0.21	0.19	0.20	N/A	N/A	N/A
Nepal	5	36	0.12	0.08	0.05	0.05	0.19	0.19	0.16	0.16	0.14	N/A	N/A	N/A
Niger	1	135	0.24	0.28	0.33	0.37	0.25	0.26	0.31	0.37	0.27	0.32	0.38	0.27

	2	160	0.20	0.21	0.20	0.20	0.19	0.19	0.18	0.20	0.19	0.18	0.16	0.19
	3	177	0.22	0.24	0.25	0.23	0.23	0.23	0.25	0.22	0.23	0.25	0.23	0.23
	4	175	0.18	0.15	0.13	0.13	0.17	0.16	0.13	0.13	0.15	0.12	0.12	0.15
	5	124	0.16	0.11	0.08	0.07	0.17	0.16	0.13	0.09	0.16	0.13	0.11	0.16
	1	190	0.27	0.38	0.44	0.45	0.24	0.28	0.32	0.34	0.25	N/A	N/A	N/A
	2	187	0.25	0.30	0.31	0.31	0.23	0.25	0.27	0.29	0.23	N/A	N/A	N/A
	3	127	0.19	0.17	0.15	0.14	0.20	0.19	0.18	0.17	0.20	N/A	N/A	N/A
	4	100	0.16	0.10	0.08	0.07	0.18	0.16	0.14	0.13	0.18	N/A	N/A	N/A
Nigeria	5	73	0.12	0.04	0.03	0.02	0.15	0.13	0.09	0.06	0.14	N/A	N/A	N/A
	1	119	0.30	0.43	0.54	0.55	0.27	0.30	0.40	0.42	0.29	N/A	N/A	N/A
	2	115	0.23	0.21	0.20	0.20	0.21	0.21	0.20	0.21	0.22	N/A	N/A	N/A
	3	98	0.19	0.18	0.14	0.14	0.20	0.19	0.18	0.18	0.21	N/A	N/A	N/A
	4	84	0.15	0.11	0.08	0.07	0.16	0.15	0.11	0.09	0.15	N/A	N/A	N/A
Pakistan	5	48	0.13	0.07	0.04	0.04	0.16	0.15	0.12	0.09	0.14	N/A	N/A	N/A
	1	119	0.25	0.26	0.30	0.33	0.23	0.23	0.27	0.31	0.25	0.29	0.35	0.25
	2	103	0.23	0.25	0.27	0.26	0.22	0.22	0.24	0.24	0.23	0.26	0.24	0.23
	3	104	0.20	0.20	0.18	0.18	0.13	0.13	0.09	0.09	0.15	0.11	0.10	0.15
	4	104	0.19	0.17	0.15	0.15	0.20	0.20	0.18	0.20	0.19	0.17	0.16	0.19
Rwanda	5	75	0.14	0.12	0.10	0.08	0.22	0.22	0.21	0.15	0.18	0.17	0.15	0.18
	1	92	0.28	0.30	0.35	0.35	0.23	0.23	0.26	0.25	0.24	0.27	0.27	0.24
	2	66	0.22	0.23	0.23	0.23	0.20	0.20	0.20	0.21	0.20	0.20	0.19	0.20
	3	67	0.21	0.21	0.20	0.20	0.21	0.21	0.22	0.21	0.21	0.21	0.22	0.21
	4	44	0.17	0.15	0.13	0.13	0.19	0.19	0.18	0.16	0.19	0.18	0.20	0.19
Senegal	5	28	0.12	0.11	0.08	0.08	0.17	0.17	0.14	0.16	0.16	0.15	0.13	0.16
	1	186	0.20	0.19	0.19	0.19	0.19	0.19	0.18	0.19	0.20	0.20	0.21	0.20
	2	177	0.23	0.24	0.28	0.29	0.22	0.22	0.25	0.25	0.24	0.27	0.32	0.24
	3	189	0.21	0.22	0.23	0.21	0.20	0.20	0.21	0.20	0.21	0.21	0.17	0.21
	4	168	0.19	0.19	0.18	0.18	0.19	0.19	0.18	0.19	0.18	0.17	0.16	0.18
Sierra Leone	5	144	0.16	0.15	0.13	0.12	0.19	0.20	0.18	0.17	0.17	0.15	0.14	0.17
Tajikistan	1	58	0.24	0.27	0.30	0.31	0.23	N/A	N/A	N/A	0.23	0.26	0.29	0.23

	2	56	0.21	0.19	0.18	0.20	0.18	N/A	N/A	N/A	0.19	0.17	0.20	0.19
	3	50	0.18	0.18	0.17	0.15	0.18	N/A	N/A	N/A	0.18	0.15	0.12	0.18
	4	36	0.19	0.18	0.18	0.17	0.21	N/A	N/A	N/A	0.22	0.24	0.22	0.22
	5	38	0.18	0.18	0.17	0.17	0.20	N/A	N/A	N/A	0.18	0.18	0.18	0.18
	1	103	0.25	0.29	0.34	0.34	0.22	0.22	0.25	0.26	0.26	0.29	0.30	0.26
	2	92	0.21	0.22	0.22	0.22	0.18	0.18	0.17	0.17	0.19	0.18	0.18	0.19
	3	91	0.20	0.23	0.21	0.23	0.20	0.20	0.20	0.21	0.20	0.20	0.23	0.20
	4	88	0.18	0.14	0.12	0.12	0.19	0.19	0.17	0.17	0.17	0.16	0.16	0.17
Tanzania	5	84	0.16	0.13	0.10	0.09	0.22	0.21	0.21	0.18	0.18	0.17	0.14	0.18
	1	87	0.23	0.31	0.34	0.36	0.22	N/A	N/A	N/A	0.24	N/A	N/A	N/A
	2	94	0.22	0.24	0.24	0.24	0.19	N/A	N/A	N/A	0.20	N/A	N/A	N/A
	3	89	0.22	0.20	0.20	0.18	0.22	N/A	N/A	N/A	0.22	N/A	N/A	N/A
	4	81	0.19	0.13	0.12	0.13	0.19	N/A	N/A	N/A	0.19	N/A	N/A	N/A
Timor-Leste	5	52	0.15	0.12	0.09	0.09	0.18	N/A	N/A	N/A	0.16	N/A	N/A	N/A
	1	120	0.25	0.23	0.25	0.25	0.23	0.23	0.25	0.27	0.26	0.30	0.28	0.26
	2	109	0.24	0.28	0.31	0.30	0.22	0.22	0.24	0.22	0.24	0.26	0.28	0.24
	3	97	0.23	0.26	0.27	0.28	0.22	0.22	0.24	0.26	0.23	0.25	0.27	0.23
	4	78	0.18	0.15	0.13	0.13	0.20	0.20	0.19	0.19	0.18	0.15	0.14	0.18
Togo	5	46	0.10	0.07	0.04	0.03	0.14	0.13	0.08	0.06	0.09	0.05	0.04	0.09
	1	123	0.23	0.23	0.24	0.24	0.19	0.19	0.18	0.19	0.22	0.22	0.22	0.22
	2	125	0.22	0.25	0.26	0.26	0.22	0.22	0.25	0.25	0.24	0.26	0.26	0.24
	3	100	0.21	0.22	0.23	0.23	0.19	0.20	0.20	0.20	0.20	0.19	0.18	0.20
	4	104	0.20	0.19	0.18	0.18	0.21	0.21	0.22	0.22	0.21	0.21	0.21	0.21
Uganda	5	72	0.14	0.11	0.09	0.09	0.18	0.18	0.15	0.14	0.14	0.12	0.14	0.14
	1	69	0.28	0.36	0.45	0.45	0.25	0.27	0.34	0.35	0.28	0.36	0.37	0.28
	2	72	0.23	0.25	0.25	0.25	0.22	0.22	0.23	0.23	0.22	0.23	0.23	0.22
	3	56	0.19	0.18	0.15	0.15	0.18	0.18	0.15	0.15	0.18	0.15	0.15	0.18
	4	46	0.17	0.13	0.10	0.10	0.18	0.17	0.15	0.15	0.17	0.14	0.14	0.17
Yemen	5	38	0.13	0.08	0.05	0.05	0.17	0.16	0.13	0.12	0.15	0.12	0.11	0.15
Zambia	1	100	0.26	0.30	0.35	0.36	0.23	0.24	0.28	0.30	0.25	0.30	0.31	0.25

	2	85	0.20	0.23	0.22	0.22	0.19	0.19	0.18	0.19	0.19	0.18	0.18	0.19
	3	79	0.19	0.19	0.18	0.18	0.18	0.19	0.17	0.18	0.19	0.17	0.16	0.19
	4	73	0.20	0.17	0.16	0.15	0.21	0.20	0.21	0.20	0.20	0.20	0.19	0.20
	5	58	0.15	0.11	0.09	0.08	0.19	0.18	0.16	0.14	0.16	0.14	0.16	0.16
	1	85	0.24	0.24	0.27	0.27	0.23	0.24	0.27	0.26	0.27	0.31	0.31	0.27
	2	88	0.23	0.27	0.28	0.29	0.23	0.23	0.25	0.26	0.24	0.26	0.26	0.24
	3	81	0.20	0.25	0.24	0.24	0.19	0.19	0.18	0.17	0.19	0.17	0.18	0.19
	4	71	0.19	0.13	0.13	0.13	0.21	0.20	0.21	0.21	0.20	0.19	0.19	0.20
Zimbabwe	5	58	0.14	0.10	0.08	0.08	0.14	0.13	0.09	0.10	0.11	0.07	0.06	0.11

Table S4.6. Sensitivity analysis – changes in the area under the curve of the distribution of cases and deaths with under-five mortality rate adjustment (U5MR)

Δ AUC: changes in the area under the curve.
Difference in Δ AUC from original results: calculated as (Δ AUC from s1 to s2 under U5MR adjustment) - (Δ AUC from s1 to s2 in the original analysis).
N/A: estimates not available due to no vaccine introduction in 2016.
Cases S1: distribution of cases under the assumption of zero vaccine coverage.
Cases S2: distribution of remaining cases after current vaccine coverage rates.
Deaths S1: distribution of remaining cases not averted by vaccine programs, under the hypothetical scenario of people not having access to any treatment.
Deaths S2: Distribution of deaths with current treatment utilization rates.
MCV: measles first dose, PCV: pneumococcal conjugate vaccine, RV: rotavirus vaccine.

	MCV				PCV				RV			
	Cases: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Deaths: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Cases: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Deaths: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Cases: Δ AUC from s1 to s2	Difference in Δ AUC from original results	Deaths: Δ AUC from s1 to s2	Difference in Δ AUC from original results
Armenia	-8	0	9	0	1	0	9	0	1	0	12	0
Bangladesh	24	0	7	0	1	0	14	0	0	N/A	12	N/A
Benin	26	-1	6	0	4	0	6	0	0	N/A	9	N/A
Burkina Faso	25	0	11	0	1	0	18	0	1	0	17	0
Burundi	10	0	1	0	0	0	3	0	0	0	1	0
Cambodia	40	-2	-2	0	3	0	0	0	0	N/A	-13	N/A
Cameroon	45	-4	7	-1	9	0	12	0	4	0	9	0
Chad	8	0	7	0	N/A	N/A	N/A	N/A	0	N/A	10	N/A
Comoros	30	0	0	0	N/A	N/A	N/A	N/A	0	N/A	-1	N/A
Congo	40	-1	5	-1	5	0	15	0	3	0	8	0
Côte d'Ivoire	24	-1	7	0	5	0	14	0	2	0	5	0
Democratic Republic of the Congo	23	-1	1	0	6	0	3	0	0	N/A	-2	N/A

Ethiopia	32	-1	6	0	8	0	15	0	4	0	14	0
The Gambia	-25	2	-2	0	-1	0	-3	0	0	0	-3	0
Ghana	11	0	-6	0	1	0	-3	0	0	0	-10	0
Guinea	16	-1	10	-1	N/A	N/A	N/A	N/A	0	N/A	14	N/A
Haiti	-1	0	10	-1	1	0	14	0	2	0	11	0
Honduras	-4	-2	2	0	0	0	7	0	0	0	0	0
Indonesia	11	0	5	1	N/A	N/A	N/A	N/A	0	N/A	0	N/A
Kenya	21	0	0	0	1	0	4	0	0	0	-6	0
Kyrgyz Republic	-11	0	13	-1	-3	0	15	0	0	N/A	22	N/A
Lesotho	10	0	-2	0	0	0	1	0	0	N/A	-9	N/A
Liberia	11	0	0	0	3	0	-4	0	1	0	4	0
Malawi	8	0	3	0	0	0	9	0	0	0	-3	0
Mali	27	-1	7	0	6	0	13	0	2	0	11	0
Mozambique	29	-1	5	0	4	0	9	0	2	0	12	0
Nepal	15	-1	3	0	2	0	6	0	0	N/A	5	N/A
Niger	23	0	10	0	5	0	22	0	3	0	11	0
Nigeria	49	-4	5	0	15	0	11	0	0	N/A	12	N/A
Pakistan	39	-2	6	-1	10	0	13	0	0	N/A	19	N/A
Rwanda	10	0	8	-1	1	0	18	0	0	0	16	0
Senegal	8	-1	-1	0	1	0	-4	0	1	0	2	0
Sierra Leone	-2	0	3	0	-1	0	3	0	0	0	10	0
Tajikistan	3	0	5	0	N/A	N/A	N/A	N/A	0	0	10	0
Tanzania	17	0	2	0	2	0	9	0	1	0	7	0
Timor-Leste	29	0	5	0	N/A	N/A	N/A	N/A	0	N/A	12	N/A
Togo	11	-2	1	-1	1	0	5	0	1	0	-1	0
Uganda	9	-1	-1	0	0	0	1	0	0	0	-6	0
Yemen	33	-1	2	0	6	0	4	0	3	0	6	0
Zambia	20	-1	3	0	3	0	9	0	1	0	1	0
Zimbabwe	18	-1	-1	0	3	0	-3	0	1	0	0	0

Table S4.7. Ranges of relative risks of risk and prognostic factors

		Cases	Deaths
Disease	Risk/prognostic factors	Point estimate and range in brackets	Point estimate and range in brackets
Measles	Wasting	z-score < -3SD: 38.0 [5.1, 200.7] -2SD < z-score < -3SD: 8.5 [1.3, 42.9]	z-score < -3SD: 38.0 [5.1, 200.7] -2SD < z-score < -3SD: 8.5 [1.3, 42.9]
	Underweight	z-score < -3SD: 5.7 [1.8, 12.4] -2SD < z-score < -3SD: 2.5 [1.3, 5.1]	z-score < -3SD: 5.7 [1.8, 12.4] -2SD < z-score < -3SD: 2.5 [1.3, 5.1]
	Stunting	z-score < -3SD: 2.5 [1.1, 6.6] -2SD < z-score < -3SD: 1.5 [1.0, 3.3]	z-score < -3SD: 2.5 [1.1, 6.6] -2SD < z-score < -3SD: 1.5 [1.0, 3.3]
	Vitamin A deficiency	2.4 [1.6, 3.5]	2.4 [1.6, 3.5]
Pneumonia	Wasting	z-score < -3SD: 116.7 [25.2, 179.3] -2SD < z-score < -3SD: 25.6 [6.1, 39.7]	z-score < -3SD: 116.7 [25.2, 179.3] -2SD < z-score < -3SD: 25.6 [6.1, 39.7]
	Non-exclusive breastfeeding	5.4 [1.0, 20.9]	2.8 [1.3, 5.2]
	Underweight	z-score < -3SD: 2.1 [1.8, 2.7] -2SD < z-score < -3SD: 1.3 [1.2, 1.4]	z-score < -3SD: 2.1 [1.8, 2.7] -2SD < z-score < -3SD: 1.3 [1.2, 1.4]
	Stunting	N/A	z-score < -3SD: 1.9 [1.0, 3.6] -2SD < z-score < -3SD: 1.2 [1.0, 1.7]
	Vitamin A deficiency	1.6 [1.2, 2.0]	1.6 [1.2, 2.0]
	Low birth weight	1.4 [1.4, 1.4]	N/A
Diarrhea	Wasting	z-score < -3SD: 105.8 [42.2, 158.0] -2SD < z-score < -3SD: 23.3 [8.9, 35.9]	z-score < -3SD: 105.8 [42.2, 158.0] -2SD < z-score < -3SD: 23.3 [8.9, 35.9]
	Unsafe sanitation	3.2 [2.8, 3.7]	3.2 [2.8, 3.7]
	Underweight	z-score < -3SD: 2.3 [2.1, 2.8] -2SD < z-score < -3SD: 1.2 [1.2, 1.3]	z-score < -3SD: 2.3 [2.1, 2.8] -2SD < z-score < -3SD: 1.2 [1.2, 1.3]
	Non-exclusive breastfeeding	1.5 [1.0, 2.3]	3.9 [1.5, 8.3]
	Stunting	z-score < -3SD: 1.9 [1.3, 2.7] -2SD < z-score < -3SD: 1.2 [1.1, 1.5]	z-score < -3SD: 1.9 [1.3, 2.7] -2SD < z-score < -3SD: 1.2 [1.1, 1.5]

SD: standard deviation.
N/A: not a risk/prognostic factor for the disease.