# IMPACT OF LARGE-SCALE HEALTH INTERVENTIONS ON POPULATION HEALTH, ECONOMIC FUNCTIONING, AND INVESTMENTS IN HUMAN CAPITAL IN SUB-SAHARAN AFRICA

Aleksandra Jakubowski

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Approved by:

Harsha Thirumurthy

Sally C. Stearns

Margaret E. Kruk

John Paul

Gustavo Angeles

## ABSTRACT

Aleksandra Jakubowski: Impact of Large-Scale Health Interventions on Population Health, Economic Functioning, and Investments in Human Capital in Sub-Saharan Africa
(Under the direction of Harsha Thirumurthy)

Donations from the United States are a major source of global health funding. The United States invests a large portion of its global health aid portfolio in bilateral aid programs which focus on combatting specific diseases in low-resource countries, including HIV and malaria. These large-scale programs have the potential not only to improve the specific diseases they target, but also to generate spillover effects to other sectors, including economic and education outcomes. Understanding the impact of large-scale programs on population-level health and their potential spillover effects is essential for learning about the returns on such investments. My dissertation investigates the impact of interventions supported with funding from two of the largest US bilateral aid programs, the President's Malaria Initiative (PMI) and the President's Emergency Plan for AIDS Relief (PEPFAR), on child mortality, economic functioning of households, and investments in human capital. This dissertation leveraged data from multiple sources, including publicly available data on child mortality and population coverage of malaria interventions from 32 countries in sub-Saharan Africa and household socio-economic data from a large community-randomized trial of a novel HIV testing and treatment strategy in Uganda and Kenya.

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## PREFACE

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| | |
|---|---|
| ACT | Artemisinin-based combination therapy |
| AIDS | Acquired Immune Deficiency Syndrome |
| AIS | AIDS Indicator Surveys |
| AOR | Adjusted Odds Ratio |
| ART | Antiretroviral therapy |
| CD4 | Cluster of differentiation 4 |
| CHC | Community Health Campaigns |
| CI | Confidence interval |
| DAH | Development Assistance for Health |
| DHS | Demographic and Health Surveys |
| DHS | Demographic and Health Surveys |
| DVL | Detectable viral load |
| FUY | Follow-up Year |
| GEE | Generalized estimating equations |
| GNI | Gross National Income |
| HIV | Human immunodeficiency virus |
| HIV- | Human Immunodeficiency Virus - negative |
| HIV+ | Human Immunodeficiency Virus - positive |
| IHME | Institute of Health Metrics and Evaluation |
| IPTp | Intermittent preventive treatment in pregnancy |
| IRS | Indoor residual spraying |
| ITNs | Insecticide treated nets |
| MAP | Malaria Atlas Project |

| | |
|---|---|
| MIS | Malaria Indicator Surveys |
| PEPFAR | United States President's Emergency Plan for AIDS Relief |
| PfPr2-10 | Plasmodium falciparum parasite rate in 2- to 10-year-olds |
| PMI | United States President's Malaria Initiative |
| PPP | Purchasing power parity |
| RR | Risk ratio |
| SEARCH | Sustainable East Africa Research in Community Health |
| SSA | Sub-Saharan Africa |
| USD | United States dollar |
| WDI | World Development Indicators |
| WHO | World Health Organization |

# CHAPTER 1: INTRODUCTION

## 1.1 Specific Aims

Although donors and local governments invest significant resources on health interventions in sub-Saharan Africa (SSA), there is limited evidence about the impact of these investments on population health and economic development. Among donors, the United States (US) government is the largest source of development assistance for health through such prominent programs as the US President's Emergency Plan for AIDS Relief (PEPFAR) and the US President's Malaria Initiative (PMI) [1-4]. Both of these programs were founded by President George W. Bush and expanded by President Barack Obama, each time with bilateral support of the US Congress. These large-scale programs have the potential to not only improve the specific diseases they target [5-7], but also to generate spillover effects to other sectors, including economic and education outcomes [8-10]. Understanding the impact of large-scale programs on population-level health and their potential spillover effects is essential for learning about the returns on such investments. This is especially relevant in view of the increasingly limited resources for healthcare, uncertainty about future funding levels, the growing burden of chronic diseases, and the persistently high burden of infectious diseases in low-resource settings. In SSA, malaria remains one of the leading causes of child mortality and HIV prevalence remains high and is on the rise in some sub-populations.

PMI has been among the main sources of funding for malaria interventions in SSA [11-13]. With an annual budget of over $600 million, PMI has focused on provision of four evidence-based malaria interventions: insecticide treated nets (ITNs) [14-16], artemisinin-based

combination therapy (ACTs) [15, 17], intermittent preventive treatment in pregnancy (IPTp) [16, 18-20] , and indoor residual spraying (IRS) [16, 21]. Despite this sizable investment, the impacts of PMI on population-level child mortality and use of the key malaria interventions have not been previously examined. Although internal and external evaluations of the program show that all-cause child mortality declined significantly within recipient countries [4, 22], more rigorous analyses using appropriate comparison groups are needed to determine whether these declines were the result of an expansion in PMI funding or other large-scale programs, national investments, or general trends in the SSA region.

PEPFAR is the largest contributor to the global fight against HIV/AIDS, with a majority of its budget allocated to providing treatment and care [23]. Historically, HIV-positive people in low-resource settings did not initiate treatment until their CD4 counts declined below a certain threshold. However, conclusive evidence about the health and prevention benefits of immediate ART initiation [24, 25] was the foundation for the 2015 WHO guidelines that recommend immediate treatment initiation for all HIV-positive people and the ambitious UNAIDS 90-90-90 targets, which call for 90% of people living with HIV to know their status, 90% of HIV-positive people to receive ART, and 90% of people on ART to reach viral suppression by 2020 [26, 27]. Some countries plan to meet the 90-90-90 targets by implementing widespread testing campaigns and universal access to ART, known as "HIV test-and-treat" strategy. The progress towards adopting test-and-treat has been slow [28], mainly due to the tremendous required investment of providing life-long medications to broader sections of the population [26, 29-31]. Since PEPFAR accounts for a large share of HIV funding in SSA, the potential cuts to PEPFAR's budget [32-34] pose a serious threat to expanding the HIV test-and-treat strategy and could undermine progress towards achieving the 90-90-90 targets.

PEPFAR has significantly improved access to HIV treatment and prevention initiatives in SSA and has led to reduced adult mortality in recipient countries [23, 35, 36]. Yet despite generally being praised as a success [23], this program's value and future commitment to fighting HIV in low-resource countries are being question [32-34]. At a time of increasing uncertainty about future funding levels of PEPFAR, we need objective evidence about the impact of early treatment initiation, including possible spillover effects to economic and education sectors. Since 2013, an NIH-funded cluster-randomized controlled trial of test-and-treat (NCT01864603) has been tracking socio-economic outcomes of the test-and-treat intervention in Uganda and Kenya. Evidence from this trial will enable us to better understand how expanded HIV testing and treatment affects economic functioning of people living with HIV, their families, and the broader communities in which they reside.

The *overarching objective* of this study was to use population-representative data and rigorous empirical methods to identify the effect of large-scale, disease-specific interventions on health and economic outcomes. Specifically, this project investigated the impact of malaria interventions on child mortality and the impact of HIV interventions on labor participation, healthcare costs and utilization, and human capital investments. The *central hypotheses* were that malaria interventions have reduced population-level child mortality and that greater access to HIV treatment has led to improved economic functioning of adults and better education outcomes of children. The specific study aims were to:

**Aim 1: Evaluate the impact of PMI on use of malaria prevention and treatment technologies and all-cause child mortality in SSA.**

*Hypothesis: PMI led to increased use of ITNs, IRS, and ACTs and reduced child mortality in recipient countries.*

**Aim 2: Evaluate employment and healthcare utilization of HIV-positive adults (and their household members) at various disease stages using baseline data from a cluster-randomized trial of test-and-treat.**

*Hypothesis: Declining health status of HIV-positive adults, determined with the use of objective measures of CD4+ T-cell counts, was associated with lower employment, more time lost from work due to illness, more care-seeking, and higher healthcare expenditures.*

**Aim 3: Evaluate the impact of HIV test-and-treat strategy on investments in human capital using longitudinal data from a cluster-randomized controlled trial of test-and-treat.**

*Hypothesis: HIV test-and-treat intervention positively impacted school attendance, primary school completion, at least some secondary school completion, and school expenditures.*

Given the significant investment donors and governments of developing countries make in health, we need objective evidence about the broader impact of these programs on population health and possible spillover effects to other sectors. While the burden of diseases such as HIV and malaria remains disproportionately high in SSA, donor assistance for health has stagnated in recent years and future funding levels are uncertain. Strong evidence about the returns on investments in health would provide important information to donors and governments as they deliberate future commitments to health interventions.

### 1.2 Significance

Between 1990 and 2014, high-income countries have disbursed $458 billion to address the high burden of disease and poorly functioning health systems in low-income countries [1]. At approximately 13 billion dollars annually, with the greatest share going to sub-Saharan Africa, the US is the largest contributor to development assistance for health. Most US funding is

disbursed through bilateral aid programs, or agreements between the US government and recipient countries that establish guidelines for funds distribution. PEPFAR, initiated in 2004, and PMI, initiated in 2006, are two of the largest US-based programs in sub-Saharan Africa. These programs have contributed to the scale-up of life-saving prevention, diagnostic, and treatment technologies in the region. My dissertation focused on evaluating the impact of interventions funded through PMI and PEPFAR on health, mortality, economic outcomes, and investments in education.

PMI has been among the main sources of funding for malaria interventions in SSA [11-13]. Yet the impact of PMI on child mortality rates and population-level coverage of key malaria interventions has not been previously examined. Internal and external evaluations of PMI reported declines in child mortality within PMI countries [22, 37], but comparison groups are needed to determine whether these reductions exceeded general trends in the region. Thus, PMI's contribution to curbing child mortality and improving population coverage of malaria interventions in SSA remained unknown. To my knowledge, this study was the first to compare trends in under-five mortality and utilization of malaria prevention and treatment technologies in PMI-recipient countries versus comparison countries before and after program implementation.

PEPFAR represents the majority of US global health portfolio and is the largest single source of funding for a specific disease, contributing more than 6.5 billion annually since 2009 towards HIV treatment and prevention [23]. One of PEPFAR's key objectives is improved access to ART. Evidence from SSA indicates that ART initiation among people with low CD4 counts, in line with historical WHO guidelines, leads to dramatically improved economic outcomes in terms of labor force participation, income, and quality of life for the individuals receiving ART [9, 38-44]. A limited number of studies have also documented benefits to

household members of treated adults, particularly in the form of reduced domestic labor burden [45] and increased school enrollment for children [46]. Furthermore, some evidence indicates that the positive impact of ART expansion also led to increased work hours of HIV-negative people whose households did not directly benefit from the treatment [47] and that ART availability significantly increased savings and investments in child schooling among HIV-negative individuals [48]. Although these studies offer persuasive evidence of the economic recovery following ART initiation for those with low CD4 counts, no study to date has assessed whether ART initiation among asymptomatic patients with high CD4 counts also generates economic benefits. Crucial to the discussion of economic benefits of test-and-treat is the hypothesis that delayed ART initiation may lead to a period of health and economic decline along with incomplete recovery even when patients adhere to ART. Thus, averting a decline of outcomes through early ART initiation may offer important benefits that extend beyond the health sector. My dissertation used data from the baseline wave of a cluster-randomized trial of test-and-treat to assess the economic functioning of HIV-positive adults along the disease spectrum. Furthermore, we capitalized on having economic data on the entire household in which HIV-positive adults resided to determine whether the disease affected economic functioning of their non-infected household members.

Economic benefits of ART may also translate to higher investments in human capital. HIV status of the mother and higher HIV prevalence in the community (even in households without HIV-infected adults) have a negative impact on child education in developing country settings [49, 50]. Improved access to ART might result in higher investment in human capital through several mechanisms, including higher life-expectancy, improved expectations for survival, more resources available for children's education, fewer children required to substitute

for adults' lost wages, and less time needed to devote to caring for ill household members [50-55]. Ultimately such economic benefits might translate to improved development of entire communities, especially in countries where HIV prevalence is high. Understanding how early access to ART affects household economic functioning, including multi-generational transfers of wealth through investments in human capital, can provide much needed evidence about the possible returns on investments in this strategy. My dissertation incorporated longitudinal data from a cluster-randomized trial to evaluate whether implementation of HIV test-and-treat in Uganda and Kenya has led to more school expenditures and higher school attainment of children in the intervention communities compared to children in control communities whose families received HIV care and treatment according existing standard of care.

The US government is the main source of funding for health interventions in the sub-Saharan region. As such, future decisions by US lawmakers about funding levels for key health focus areas, including HIV and malaria, carry crucial importance for the global community's ability to reduce the burden of diseases in developing countries. Aside from the clear humanitarian value of programs such as PMI and PEFAR, the success of US-funded global health aid promotes American interests and values, in line with the current administration's priorities expressed in the 2018 US budget proposal [56, 57]. For example, further investments in health aid have the potential not only to provide humanitarian relief but also to stimulate economic development of countries in SSA, which may create new and exciting trade opportunities for the United States. My dissertation aims to fill important gaps in the literature about the effectiveness of large-scale programs on recipient populations' health outcomes, economic functioning, and investments in human capital. Findings from this study can inform

future policy decisions about continued funding levels for PMI and PEPFAR and about investments in HIV test-and-treat strategies in low-income countries.

### 1.3 Innovation

The three studies conducted as part of my dissertation fill important gaps in the literature. Reducing under-five mortality is the key target of PMI, yet to date no study has established whether the declining trends in child mortality that have been observed within PMI-recipient countries exceed those in non-recipient countries. This study provides evidence about the impact of PMI on child mortality trends and on population coverage of malaria interventions in sub-Saharan Africa. The existing studies that point to the many benefits of treating people with HIV are based on samples of HIV-positive people in low-income countries who did not begin treatment until their health status declined below a certain threshold (due to historical guidelines). Thus, most studies to date have been based on people who experienced an economic decline as they awaited ART initiation. My dissertation used data from a large cluster-randomized trial of test-and-treat in Uganda and Kenya to assess employment and health seeking behaviors of HIV-positive people along the disease spectrum, including asymptomatic people with high CD4 counts. Furthermore, because we collected data on entire households in the study communities, I was also able to track the economic functioning of other people in the household who resided with HIV-positive individuals at various disease stages. This innovative design enabled me to establish how HIV-disease progression affects entire families that are impacted by HIV-infection of a household member. The ability to track the same households over time also enabled me to establish the causal impact of expanded HIV test-and-treat intervention on human capital investments, an area of research that has not yet been explored in the literature.

While many studies rely on a single source of data, my dissertation leveraged data from multiple sources, including publicly-available data from 32 countries in SSA and cluster-

randomized controlled-trial data from Uganda and Kenya. First, to investigate the impact of PMI on population-level health, I combined multiple datasets to incorporate child mortality data (from the Demographic and Health Surveys, AIDS Indicator Surveys and Malaria Indicator Surveys [58]), health aid donations from wealthy countries (from the Institute of Health Metrics and Evaluation [59]), population coverage of malaria prevention and treatment interventions (from the Malaria Atlas Project [15]), and general country characteristics (e.g. from the Word Banks's World Development Indicators [60] and Worldwide Governance Indicators [61]). The combined dataset included nearly two decades of data from 32 sub-Saharan countries, which enabled me to identify PMI's contribution to the declining trends in child mortality while accounting for general mortality trends in SSA and all baseline characteristics of the study countries. The long follow-up also enabled me test key assumptions of the models and perform multiple sensitivity analyses to test robustness of study findings.

Impact of PMI was estimated using both a time-varying binary measure of receipt of PMI funding in a given country (extracted from reports to Congress) and a time-varying continuous measure of per-capita PMI funding in a given country (obtained from IHME). The per-capita aid measures addressed the possibility that program activities varied in scope between countries and within countries over time. Relying on disbursed dollars rather than committed dollars provided greater confidence that the exposure measure was correlated with interventions that reached populations in PMI countries. Furthermore, models controlled for the presence and scale of other large-scale donors (including PEPFAR and the Global Fund) that were operating in the study countries at the same time.

Second, I used data from the Sustainable East Africa Research in Community Health (SEARCH) HIV test-and-treat cluster randomized controlled trial (NCT01864603). The

SEARCH trial consists of 32 study communities, 16 of which were randomized to receive the test-and-treat intervention, which incorporated population-wide community health campaigns that include HIV tests, ART initiation offered to all HIV-positive people upon diagnosis, and streamlined care approach that reduces many barriers to linking and retaining patients in treatment. The 16 control communities followed country guidelines for HIV testing, ART initiation, and healthcare delivery. Randomized controlled trials are the gold standard for evaluating causal impact of interventions on target populations. Using randomized controlled trial data enabled me to make causal inference about the impact of early ART start on household investment in human capital. Evidence from this study will be of interest to donor and local governments that are contemplating implementing test-and-treat strategy as the national policy for HIV testing, care, and treatment.

### 1.4 Theory

This dissertation is motivated by standard human capital theory developed by Gary Becker and Yoram Ben-Porath. Human capital (traits such as health, cognition, knowledge, values, skills, and abilities) accumulates over the lifetime and has important implications for one's own health and earning potential, as well as intergenerational transfers of wealth. Most investments in human capital are made early in one's lifetime, since the "cost" of foregone wages is the lowest then and young people have a longer time to gain returns on these investments [51, 52]. Health, a particularly important component of human capital, can be considered a commodity in terms of consumption (disutility from sick time) and investment (productivity gains from healthy time). Maintaining good heath requires making investments and comes at a cost, as time spent producing good health is time spent away from work and leisure activities [62]. Education, another key component of human capital, also requires monetary and time investments. Good health and education are linked, as good health is required to obtain

education, more educated people have better health and demand less medical care, and healthy and more educated adults (particularly mothers) tend to have healthier and more educated children [55, 62, 63]. Furthermore, lower life-expectancy due to high burden of disease could lower human capital investments, as individuals with shorter time horizons can expect smaller returns on investments (either for themselves or for their children) than people who expect to live longer [51, 52, 55].

In SSA, the long-run economic costs of the HIV epidemic have been devastating. HIV/AIDS has destroyed the human capital of many adults in their prime-age, and left many children orphaned, which in turn lowered investments in their human capital development [50, 53, 54, 64-69]. This process has led to lower investments in the following generation's human capital, trapping families in a vicious cycle that stymied economic development [70]. Like HIV, malaria also negatively impacts human capital accumulation, lowers earning potential in adulthood, and impedes economic development [71-74]. In utero and during childhood, contracting malaria may cause cognitive impairments, severe illness and school absenteeism, or in the worst case, death [75-78].

This dissertation focuses on the link between health and human capital development. First, I investigated whether PMI's investments in malaria interventions have resulted in lower child mortality trends in SSA. Second, I evaluated the link between HIV disease progression and economic outcomes of adults. Households where adults fall ill are faced with the dual burden of reduced labor supply and increased costs of healthcare seeking. Given these income shocks, households may lower their investments in human capital, as they ask children to substitute for lost labor and effectively reduce time spent on education [79-81].

Prior work in the context of the HIV epidemic in SSA has documented associations between HIV and poor education outcomes, as well as links between ART and improved education outcomes [48, 50, 66, 70, 82-84]. Yet these studies relied on populations of HIV-positive people whose economic functioning declined as they awaited treatment initiation. In the third aim of my dissertation, I evaluated the impact of early access to treatment on investments in human capital. Early access to HIV interventions might have an important impact on people's ability to earn and be productive, their longevity and subjective life-expectations, and ultimately may alter how much people invest in future generations. Such economic benefits might in turn lead to improved economic development at the macroeconomic level [71, 85-87].

### 1.5 Guide to Dissertation

The remainder of this dissertation proceeds as follows. Chapter 2 provides the results from the study on PMI and child mortality in sub-Saharan Africa. Chapter 3 explores the association between economic outcomes and HIV disease progression using data from the baseline wave of the SEARCH trial. Chapter 4 evaluates the impact of test-and-treat on human capital investments using longitudinal data from the SEARCH trial. Chapter 5 includes concluding remarks.

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# CHAPTER 2: THE US PRESIDENT'S MALARIA INITIATIVE AND UNDER-5 CHILD MORTALITY IN SUB-SAHARAN AFRICA: A DIFFERENCE-IN-DIFFERENCES ANALYSIS[1]

## 2.1 Overview

**Background:** Despite substantial financial contributions by the United States President's Malaria Initiative (PMI) since 2006, no study has carefully assessed how this program may have affected important population-level health outcomes. We utilized multiple publicly available data sources to evaluate the association between introduction of PMI and child mortality rates in sub-Saharan Africa (SSA).

**Methods and findings:** We used difference-in-differences analyses to compare trends in the primary outcome of under-5 mortality rates and secondary outcomes reflecting population coverage of malaria interventions in 19 PMI-recipient and 13 non-recipient countries between 1995 and 2014. The analyses controlled for presence and intensity of other large funding sources, individual and household characteristics, and country and year fixed effects.

PMI program implementation was associated with a significant reduction in the annual risk of under-5 child mortality (adjusted risk ratio [RR] 0.84, 95% CI 0.74–0.96). Each dollar of per-capita PMI expenditures in a country, a measure of PMI intensity, was also associated with a reduction in child mortality (RR 0.86, 95% CI 0.78–0.93). We estimated that the under-5 mortality rate in PMI countries was reduced from 28.9 to 24.3 per 1,000 person-years.

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Population coverage of insecticide-treated nets increased by 8.34 percentage points (95% CI 0.86–15.83) and coverage of indoor residual spraying increased by 6.63 percent- age points (95% CI 0.79–12.47) after PMI implementation. Per-capita PMI spending was also associated with a modest increase in artemisinin-based combination therapy coverage (3.56 percentage point increase, 95% CI −0.07–7.19), though this association was only marginally significant (p = 0.054). Our results were robust to several sensitivity analyses. Because our study design leaves open the possibility of unmeasured confounding, we cannot definitively interpret these results as causal.

**Conclusions:** PMI may have significantly contributed to reducing the burden of malaria in SSA and reducing the number of child deaths in the region. Introduction of PMI was associated with increased coverage of malaria prevention technologies, which are important mechanisms through which child mortality can be reduced. To our knowledge, this study is the first to assess the association between PMI and all-cause child mortality in SSA with the use of appropriate comparison groups and adjustments for regional trends in child mortality.

## 2.2 Introduction

At the turn of the millennium, malaria was the leading cause of child mortality in sub-Saharan Africa (SSA), claiming 694,000 child lives annually [1] and accounting for nearly a quarter of all under-5 deaths [2]. Reducing child mortality and lowering the burden of malaria were central components of the Millennium Development Goals and the key mission of the Roll Back Malaria Partnership [3, 4]. Since then, under-5 mortality has declined substantially in SSA, with all-cause child mortality rates declining from an estimated 158 deaths per 1,000 live births in 2000 to 82 deaths per 1,000 live births in 2015 in malaria-endemic countries, when malaria fell to the fourth leading cause of child deaths in SSA [1]. Understanding the role global policies and funding played in reducing malaria mortality, including changes in heath behaviors, can be

valuable as countries and global donors work toward the Sustainable Development Goals, including the goal of eradicating malaria by 2030. While external funding remains a significant source of total health expenditures in low-income countries [5], health aid donations have stagnated since 2010 and future funding is surrounded by uncertainty [6]. The increasingly limited resources for healthcare delivery in developing countries demand strong evidence on the most effective and efficient ways to provide life-saving, evidence-based prevention and treatment interventions to vulnerable populations.

The US President's Malaria Initiative (PMI), launched in 2005 by President George W. Bush and expanded by President Barack Obama, has been among the main sources of funding for malaria interventions in SSA [1, 6, 7]. With an annual budget of over $500 million since 2010 [8], PMI has primarily focused on provision of 4 recommended, evidence-based malaria interventions: insecticide-treated nets (ITNs) [9-11], rapid diagnostic tests and artemisinin-based combination therapy (ACTs) [10, 12], intermittent preventive treatment in pregnancy (IPTp) [11, 13-15], and indoor residual spraying (IRS) [11, 16]. Despite this sizable investment, the association between PMI, child mortality rates, and population-level coverage of key malaria interventions has not been previously examined.

While PMI program evaluations show that all-cause child mortality declined significantly in recipient countries [8, 17, 18], comparison groups are needed to determine whether these reductions were due to expansion in PMI funding or other interventions instead, including programs supported by the Global Fund for HIV/AIDS, Tuberculosis, and Malaria (Global Fund henceforth), the President's Emergency Plan for AIDS Relief (PEPFAR), or domestic investments. Previous studies have documented higher access to ITNs, ACTs, and IRS coverage in PMI-recipient countries [19-22] but have not compared these trends to non-recipient countries.

More rigorous analysis of the association between PMI and key outcomes is needed to assess whether PMI was successful at curbing child mortality through implementation of evidence-based malaria interventions. We used data from 32 sub-Saharan countries spanning nearly 20 years to determine the association between PMI and all-cause child mortality rates as well as malaria prevention and treatment behaviors.

**2.3 Methods**

PMI began as a small program in 2006 with funding initially going to 3 countries and an annual budget of $30 million. Within 2 years, PMI scaled-up to 15 focus countries and had an annual budget of $300 million. By 2011, PMI expanded to 19 countries in SSA (Angola, Benin, Democratic Republic of Congo, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Tanzania, Uganda, Zambia, and Zimbabwe) and had an annual budget of $600 million. Approximately 40% of PMI's budget has been allocated to procurement of commodities to prevent, diagnose, and treat malaria [8]. Since its inception, PMI has also focused on building capacity through training of healthcare workforce, providing technical support, and strengthening supply chain systems.

PMI country selection was based on several criteria, including high malaria burden, government capacity, potential for impact, willingness to partner with US government, national malaria control policies consistent with the World Health Organization standards, and other donor involvement in malaria control. Yet these criteria do not fully explain country selection. Some countries with relatively low malaria prevalence were selected (e.g., Ethiopia at 3.4% *Plasmodium falciparum* parasite rate in 2- to 10-year-olds [$Pf Pr_{2-10}$] in 2005 and Zimbabwe at 2.5% $Pf Pr_{2-10}$ in 2005) whereas others with high malaria burden were not selected (e.g., Cameroon at 47.0% $Pf Pr_{2-10}$ in 2005 and Burkina Faso at 55.4% $Pf Pr_{2-10}$ in 2005). Cameroon and Burkina Faso also score higher on World Bank's Worldwide Governance Indicators than do

Ethiopia and Zimbabwe. Thus, while selection process of PMI-recipient countries was not random, it does not appear to have been systematically associated with malaria burden, governance, or health system performance. The analyses carried out in this study, described below, include comparisons of recipient and non-recipient countries as well as tests for differential impacts based on initial country characteristics.

### 2.3.1 Measures

#### 2.3.1.1 Child mortality data

Child mortality data were obtained from 77 Demographic and Health Surveys (DHS), 14 Malaria Indicator Surveys (MIS), and 5 AIDS Indicator Surveys (AIS) in 32 countries in SSA. DHS, MIS, and AIS are nationally representative, cross-sectional surveys that include common questions about birth dates and survival status of all births to women of reproductive age (15–49 years) [23]. From these data, we constructed a longitudinal cohort with annual observations for each live birth between 1995 and 2014. We used information about the year of child's birth, whether each child was alive at the time of the survey, and how old a child was if s/he died to define the primary outcome, which was a binary indicator of mortality in each year. We also extracted data about the child's age and gender, mother's age, mother's education, mother's parity, household wealth, whether the head of household was female, and whether the household was in rural area. We excluded from the analysis malaria non-endemic countries (Lesotho), small island countries (Comoros, Sao Tome, and Principe) and South Africa, because only one DHS from 1998 was available there. Additional details about data structure are described in Appendix 1.

#### 2.3.1.2 Malaria interventions coverage data

Secondary outcomes were defined based on country-level annual data about population coverage of key malaria prevention and treatment interventions, which we obtained from the Malaria Atlas Project (MAP) [24]. MAP estimates of ITN, ACT, and IRS coverage are based on household-level data from DHS, MIS, Multiple Indicator Cluster Surveys, AIS, Malaria and Anemia Prevalence Survey, and the World Health Organization, combined with national malaria control program data from 43 countries between 2000 and 2015 [10]. The ITN estimate represents the proportion of people who slept under an insecticide-treated bednet on any given night each year; the ACT estimate represents the proportion of fever cases in under-5-year-olds receiving ACTs; and the IRS estimate represents the proportion of the population protected by IRS of insecticides. We did not find reliable data on rapid diagnostic tests and IPTp.

#### 2.3.1.3 Exposure to PMI and other health aid

We measured receipt of donor funding by individual countries with 2 measures: a binary indicator of whether a program provided funding to a given country in a given year and a continuous measure of program intensity using per-capita disbursements in a given country and year. The binary indicators of program activity were extracted from reports to US Congress. The per-capita aid measures address the possibility that program activities vary in scope between countries and within countries over time. These country-year data were obtained from publicly available Development Assistance for Health 1990–2014 dataset, compiled by the Institute for Health Metrics and Evaluation (IHME) [25]. We excluded 2013–2014 disbursements from the analysis, as these data were not complete due to reporting lags. The IHME dataset distinguished between the funding source (country of origin), the distribution channel (bilateral versus multilateral versus private foundations), health focus area, and the recipient country. Using these characteristics, we divided total development assistance for health into 6 categories (details in the

Appendix 1): PMI (US bilateral aid for malaria); Global Fund malaria aid; other malaria aid; PEPFAR (US bilateral aid for HIV/AIDS); Global Fund HIV/tuberculosis aid; and all other health disbursements. These 6 categories summed to 100% of development assistance for health provided to SSA that were captured in IHME's dataset. All health disbursements in this study are reported in 2014 US dollars.

### 2.3.2 Statistical analyses

We performed difference-in-differences analysis by estimating regression models that compared trends in outcomes in PMI recipient counties to trends in comparison countries while adjusting for country fixed effects, which controlled for underlying differences between countries, and year fixed effects, which controlled for secular trends in outcomes. We evaluated the primary outcome of annual child mortality risk using modified Poisson regression models [26] with robust standard errors clustered at the country level to relax the assumption of independently and identically distributed error terms [27, 28]. The proportion of population covered by ITN, IRS, and ACT outcomes were evaluated using ordinary least squares regression models, with robust standard errors. Statistical significance threshold was set at alpha = 0.05 using two-tailed tests. We used child-year data from the DHS, MIS, and AIS to estimate how binary indicators of program activity were associated with annual risk of mortality among children aged <5 years. The first model included a binary indicator of PMI funding in a given country and year (Model 1 in Appendix 1). The second model added binary indicators for whether countries received funding from other large-scale donors in each year, namely the Global Fund and PEPFAR (Model 2). The third model also added individual and household characteristics (Model 3); observations with missing data were dropped from analysis. We then re-fitted these 3 models using our continuous measures of program intensity, or per-capita aid disbursements, instead of the binary funding indicators (Models 4–6). A similar analytical

strategy was undertaken in a previous study that sought to estimate the effect of PEPFAR on adult mortality in SSA [29].

Country-level MAP data were then used to evaluate the association between binary indicators of PMI, PEPFAR and Global Fund, and population-coverage of ITNs, ACTs, and IRS, while controlling for total population size (Model 7). Next, we explored the associations between per-capita measures of program intensity and malaria intervention coverage, again controlling for population size (Model 8). Finally, we tested whether the associations between PMI and health-related outcomes varied over time by including a series of binary indicators for each year in which PMI, Global Fund, and PEPFAR funds were available in a country (Models 9 and 10). These models were used to test the mechanism though which introduction of PMI funding might have shifted trends in malaria incidence and under-5 mortality rates.

The difference-in-differences design is a quasi-experimental method that relies on the assumption that, in the absence of any intervention, countries receiving PMI funding would have identical trends in outcomes as non-recipient countries. We tested this "parallel trends" assumption by using data from pre-PMI years and estimating models that included an interaction term between an indicator of PMI country and a linear time trend (Model 11). In order to assess whether countries were selectively chosen for PMI, we also compared the average baseline performance on the available measures of governance and health systems between PMI recipient and comparison countries.

We performed several sensitivity analyses to verify our results. First, we excluded deaths that occurred in the first month of the child's life to confirm that results were not driven by reductions in neonatal mortality. Reductions in neonatal mortality could be attributed to better prenatal and delivery care rather than malaria interventions. Second, we tested whether the

association between PMI and child mortality was stronger in rural areas where malaria burden is generally higher. Third, we separately excluded each individual country from the analysis to ensure that results were not driven by patterns in any single country. Fourth, we assessed whether results were robust to excluding the Democratic Republic of Congo and Nigeria because PMI programs were implemented at subnational levels in these 2 countries and under-5 mortality rates due to malaria were especially high there [30]. Fifth, we assessed whether the results were robust to the type of model chosen by also estimating logit, probit, and Cox regression models. Next, we confirmed that the parallel trends assumption held when we interacted a nonlinear time trend with PMI program indicators using data from pre-PMI years. Finally, we confirmed that we were able to detect the association between PMI and malaria intervention coverage using alternative data sources.

**2.4 Results**

The child mortality sample from DHS, MIS, and AIS included 7,752,071 child-year observations, of which 5,837,998 (75%) were from 19 PMI-recipient countries and the remaining 1,914,073 (25%) were from 13 comparison countries (Table 2.1). Approximately 9.44% of the 2,112,951 children in our sample died before reaching age 5. In PMI countries, we observed 148,551 child deaths during the study period (under-5 mortality rate 25.4 per 1,000 person-years) while in comparison countries we observed 50,930 child deaths (under-5 mortality rate of 26.6 per 1,000 person-years). Detailed information about program start years, survey years, and sample size by study country are provided in Table A of Appendix 1. Characteristics of children and mothers in the sample did not significantly differ between PMI recipient and non-recipient countries, with 2 exceptions: fewer women in PMI countries disclosed having no education and a larger share of children in PMI countries lived in rural areas (Table B in Appendix 1). The data

on coverage of malaria-related interventions included 512 country-year observations, of which 304 (59%) were from PMI countries and 208 (41%) from comparison countries.

We found no major differences between PMI and comparison countries in baseline malaria burden, child mortality rates, and indicators of health system performance or governance (Table 2.2). While there was considerable variation across countries in baseline malaria burden, the average rate of *P. falciparum* in 2- to 10-year-olds in 2005 was approximately 30% in both study groups. The World Bank's estimates of under-5 mortality rates [31] in 2005 were 121 per 1,000 live births in PMI countries and 128 per 1,000 live births in comparison countries (Table 2.2 and Table C in Appendix 1). PMI countries had lower baseline health expenditures, fewer nurses and midwives, and fewer physicians than comparison countries, but these differences were not statistically significant. Both study groups had negative (i.e., unfavorable) scores on government effectiveness, political stability, and corruption measures, and the differences between groups in these scores were not statistically significant. PMI countries had larger ($p$ = 0.03) and less wealthy ($p$ = 0.052) populations at baseline. Country-level baseline under-5 mortality rates, $PfPR_{2-10}$ transmission rates, and coverage of ITNs, ACTs, and IRS are listed in Table C in Appendix 1. PMI recipient countries had higher ITN coverage at baseline, but ACT and IRS coverage was approximately the same in 2005 between the study groups. Our study design adjusts for baseline differences between countries.

The test of parallel trends showed that, after controlling for baseline country characteristics, secular time trends and individual characteristics, child mortality rates in PMI recipient and non-recipient countries were identical *before* the start of the PMI program (risk ratio [RR] 1.00, 95% CI 0.98–1.01; Table 2.3). Mortality rates were declining in all of the study

countries during this time period (RR 0.96, 95% CI 0.95–0.97), but there was no evidence of trends being different between PMI and comparison countries.

PMI countries received an average of US$0.98 per-capita from US bilateral aid for malaria annually (Figure 2.1). The Global Fund provided about twice as much aid to the sub-Saharan region as PMI, with about half of the disbursements sent to PMI-recipient countries (average of US$0.89 per capita since 2006) and the other half to non-recipient countries (average of US$1.01 per capita since 2006). PMI countries received slightly more malaria funding from all other sources than non-PMI countries (US$0.26 USD versus US$0.11, respectively, since 2006), though all other malaria aid summed to less than $0.50 per-capita at its highest level. The upward trend in ITN coverage was apparent during the study period, with larger increases observed in PMI countries. ACT coverage remained fairly low in all countries and did not differ between PMI recipient versus non-recipient countries. While average IRS coverage increased in PMI countries soon after the program was introduced, this trend was not sustained, and by 2012 average coverage in the 2 study groups was again overlapping.

The average annual risk of mortality among children aged <5 years was 15% lower after the introduction of PMI (Table 2.4, Panel A; risk ratio [RR], 0.85, 95% confidence interval, CI, 0.74–0.96). Result was slightly more pronounced, at 16% reduction in mortality, after adjusting for the presence of other funding sources in a country (RR 0.84, 95% CI 0.74–0.95) and in the fully adjusted model that included individual characteristics (RR 0.84, 95% CI 0.74–0.96). The main study finding of a 16% reduction in the annual risk of child mortality after adjustment for covariates amounts to a change in the mortality rate from 28.9 per 1,000 person-years in PMI countries before program implementation to 24.3 per 1,000 person-years after implementation. Per-capita measure of PMI intensity showed that each additional dollar disbursed through PMI

was associated with a reduction in the annual risk of under-5 mortality (Table 2.4, Panel B; RR 0.84, 95% CI 0.77–0.90). After adjusting for other funding sources and individual-level covariates, PMI was associated with 14% annual reduction in under-5 mortality (RR 0.86, 95% CI 0.79–0.93). Per-capita Global Fund disbursements were marginally associated with lower risk of under-5 all-cause mortality (RR 0.96, 95% CI 0.93–1.00) in the fully adjusted models. Mortality risk was lower for females, children with more educated mothers, and children living in wealthier households and in urban areas (Tables D and E in Appendix 1); children between first and second birthdays faced the highest risk of mortality.

PMI was also associated with 8.34 percentage point increase in ITN coverage (95% CI 0.86–15.83) and 6.63 percentage point increase of IRS coverage (95% CI 0.79–12.47), as shown in Panel A of Table 2.5. When we examined PMI on the basis of program intensity (Table 2.5, Panel B), each additional per-capita dollar disbursed through PMI was associated with 4.29 percentage point annual increase in ITN coverage (95% CI 0.54–8.03) and 3.56% increase in ACTs (−0.07–7.19), though this association was only marginally significant ($p = 0.054$). Despite the relatively small amount of malaria funds disbursed through channels other than PMI and Global Fund, we found that ITN coverage increased by 9.69 percentage points (95% CI 3.41–15.97) in countries that received funding through these channels. When the study sample was expanded beyond the 32 study countries that had DHS/MIS/AIS child mortality data (i.e., to other countries in SSA that also had MAP data), we found that PMI was associated with even larger increases in ITN, ACT, and IRS coverage (Table F in Appendix 1).

We used estimates from prior studies to calculate the predicted reductions in all-cause child mortality based on the PMI-associated increases in ITN, ACT, and IRS coverage reported in Table 2.5. Our calculations incorporated evidence from Kenya, where Fegan et al. (2007)

estimated that increasing ITN coverage from 7% to 67% was associated with 44% reduction in all-cause child mortality [32]. Given the limited evidence about the impact of IRS on child mortality [16], we followed the example of Eisele et al. (2010) and assumed that IRS coverage had approximately equal protective effect to ITNs [11]. Finally, we used evidence from Zanzibar, where Bhattarai et al. (2007) found that reaching high coverage of ACTs (we used the conservative assumption that this implied full coverage) was associated 52% reduction in child mortality [33]. Applying these effect sizes to the estimates in Table 2.5, we determined that the increased coverage of these 3 prevention and treatment modalities could account for a 12.5% reduction in all-cause child mortality (additional details are in Appendix 1).

Figure 2.2 displays the association between PMI and child mortality over time and the association between PMI and coverage of malaria interventions over time. We found that as the number of years of PMI implementation rose, there were larger associated reductions in mortality rates in PMI countries and larger associated increases in coverage of ITNs. In the first year of PMI implementation, the association between the program and child mortality was small and not statistically significant (RR 0.93, 95% CI 0.86–1.01) but in subsequent years the association increased considerably (RR 0.73, 95% CI 0.61–0.88 in year 4 and RR 0.65, 95% CI 0.48–0.88 in year 5). The coefficients in year 7 and 8 have wide confidence intervals because they are based on a much lower number of observations due to fewer countries having been enrolled at the start of PMI in 2006 and fewer DHS surveys available from the later years. Similarly, the association between PMI and ITN coverage began as a small increase, but by the fifth year of PMI, the association increased to 9.5 percentage points (95% CI 2.8–16.2) and reached a peak of approximately 17 percentage point increase in years 7 and 8 (95% CI 7.5–25.6 and 5.6–29.2, respectively). IRS coverage was increasing in PMI-recipient countries up to the

fourth year of program implementation, at which point it dropped off considerably. ACT coverage increased at very moderate levels in PMI countries throughout this program's history.

We tested the robustness of study results with a series of sensitivity analyses. When neonatal deaths (i.e., those that took place within the first month of a child's life) were excluded from the analysis, the association between PMI and all-cause child mortality rate was magnified from RR 0.84 to a RR of 0.79 (95% CI 0.69–0.90) and each additional per-capita dollar spent through PMI was associated with 0.83 lower risk of mortality (95% CI 0.75–0.92), results listed in Table H in Appendix 1. Reductions in child mortality were especially evident in rural areas, where malaria burden is typically the highest and where access to malaria interventions has the higher potential for impact (Table I in Appendix 1). The annual risk reduction of child mortality was 0.83 (95% CI 0.73–0.95) in rural areas compared to 0.87 (95% CI 0.76–1.00) in urban areas. Each additional per-capita dollar disbursed through PMI was associated with 0.85 lower risk reduction of mortality in rural areas (95% CI 0.78-0.93) compared to 0.88 (95% CI 0.82-0.93) in urban areas. Results were also robust to excluding individual countries, to excluding Democratic Republic of Congo and Nigeria from the model (Table J in Appendix 1), and to different model specifications (Table K in Appendix 1). We confirmed that the parallel trends assumption held when we interacted nonlinear time trend with PMI indicators (Table L in Appendix 1). Finally, we confirmed out study finding that PMI was associated with increased utilization of ITNs using alternative data sources (Table M in Appendix 1).

**2.5 Discussion**

This study evaluated the association between PMI and population health using methods that controlled for various confounding factors. PMI was associated with large and statistically significant reductions in all-cause mortality rates among children under 5 years of age. These findings persisted in models that controlled for the presence and size of funding from other

important programs, time-invariant country characteristics, common time trends, and various individual and household characteristics. Among other funders, disbursements through the Global Fund were also modestly associated with all-cause child mortality rates. The results suggest that PMI's investment in key malaria interventions was associated with significant increases in population coverage of malaria prevention and treatment technologies, which ultimately may have contributed to the significant reductions in under-5 mortality in SSA.

The main findings indicate that PMI was associated with a 16% decline in annual risk of all-cause under-5 mortality. Furthermore, the association between PMI and child mortality was more pronounced over time. These reductions were above and beyond the declines in child mortality that were observed in PMI and non-PMI countries prior to the introduction of PMI, as well as trends in mortality that were observed in non-PMI countries in the years after introduction of PMI. The 16% relative risk reduction translates to a decline in under-5 mortality rate from 28.9 to 24.3 deaths per 1,000 person-years after PMI implementation. Because the primary outcome in this study was all-cause child mortality rate, it is important to underscore that not all of the under-5 deaths averted in PMI countries were due to malaria prevention and treatment. Nonetheless, we believe the findings that coverage of various malaria prevention and treatment interventions—including ITNs, ACT, and IRS—increased in the years after PMI introduction provide a plausible mechanism for the decline in child mortality that was associated with PMI.

### 2.5.1 Possible mechanisms

We examined existing evidence on the effectiveness of malaria interventions to assess whether the PMI-associated declines in child mortality were plausible [11, 32]. The widespread distribution of ITNs has previously been described as the most important malaria intervention in Africa [1, 34], accounting for 68% of the decrease in *P. falciparum* transmission rates between

2000 and 2015 [10]. A systematic review of efficacy trials from SSA found that use of ITNs reduced under-5 mortality by about a fifth [9]. An observational study in Kenya found that after mass distribution and promotion of ITNs, increased bednet use was associated with a 44% reduction in child mortality [32]. Consistent with other studies, we found that ITN coverage increased considerably in SSA since the turn of millennium, and that coverage was above average trends in PMI-recipient countries. Thus, our finding that PMI was associated with higher ITN coverage can partially explain the main finding regarding child mortality rates. We also found that PMI was associated with higher IRS coverage, particularly in the first few years of PMI program activities. Existing evidence shows that ITN and IRS coverage implemented together might have increased effectiveness, especially in high transmission areas with moderate ITN coverage [11, 21, 35]. Together, the rising coverage of ITNs and IRS may have offered an even greater protective effect on malaria burden and, ultimately, child mortality rates in PMI countries. Evidence also suggests that high coverage of ACTs may result in significant reductions in child mortality [33]. While the association between PMI and ACT coverage in our study was very modest, it is possible that higher access to malaria treatment might have made some, albeit small, contribution to the reduction in all-cause mortality. Our calculations showed the PMI-associated increases in ITN, IRS, and ACT coverage could account for a 12.5% reduction in all-cause child mortality. However, this result should be interpreted with caution given that we had to make several assumptions in our calculations and that we applied estimates from 2 specific settings to 32 different countries in SSA. Our calculations also did not account for interactive effects between ITNs, IRS, and ACTs or the fact that the increases in coverage detected in our study were considerably smaller in magnitude than those that were assumed or estimated in the other studies.

Other malaria interventions supported with PMI funds that were not assessed in this study, such as rapid diagnostic tests and IPTp, could have also contributed to reducing malaria burden and lowering all-cause child mortality rates. Protecting pregnant women from malaria in particular has been shown to lead to better birth outcomes and decreased risk of developing malaria, acute respiratory infection, and diarrhea during childhood, the leading causes of child deaths in SSA today [36, 37]. Finally, it is possible that introduction of PMI funds for malaria freed up domestic resources for other health interventions that further contributed to the reduction in all-cause child mortality. For instance, PMI invests in health systems strengthening and capacity building of laboratories and pharmaceutical chain systems. HIV programs have been found to have positive spillover effects to the broader health systems [38, 39], and it is possible that similar synergies exist between malaria-specific interventions and general health system functioning.

Internal and external evaluations of PMI have documented declines in under-5 mortality in PMI-recipient countries and concluded that the program was successful in making significant progress towards reducing child mortality [8, 18]. Our study provides additional evidence in support of this conclusion and extends the existing literature by using a quasi-experimental design. Despite PMI's achievements, population coverage of key malaria interventions remained low throughout most of the African region [40]. As of 2015, most PMI countries were under target for key populations sleeping under ITNs and timely access to diagnostic tests and malaria medicines [8]. Furthermore, PMI has scaled down or even suspended IRS in some countries after worrying reports of resistance to insecticides have emerged [41, 42] and cost of other insecticides increased substantially [43]. The drop in IRS coverage in PMI recipient countries can be clearly seen in Figure 2.1 and Figure 2.2. Bearing in mind that detecting population-level

changes in ACT and IRS coverage can be difficult due to more targeted implementation, coverage of these interventions remained quite low throughout the study period, and increases in coverage after PMI implementation were also modest. As further support for malaria interventions is considered, health systems strengthening will be necessary to deliver more complicated interventions such as diagnostic tests and ACT, which require interacting with the healthcare system and a well-functioning drug supply chain system.

### 2.5.2 Strengths and limitations

The reliance on 2 different measures of PMI activity and various robustness tests strengthened our confidence in the main study findings. It is reassuring that an association between PMI and the primary and secondary outcomes was detected using both a time-varying binary measure of receipt of PMI funding by a country (extracted from reports to Congress) and a continuous measure of per-capita measure of PMI funding obtained by countries in each year (obtained from IHME). Relying on disbursed dollars rather than committed dollars provided greater confidence that the exposure measure was correlated with interventions that reached populations in PMI countries. Confidence in the study findings was further strengthened by the robustness of results to adjustments for expenditures from all other funding sources captured in the IHME dataset. We were also reassured that exclusion of neonatal deaths, which could be attributed to better prenatal and delivery care rather than malaria interventions, amplified the magnitude of the association between PMI and child mortality. In addition, the data on coverage of malaria interventions were adjusted for geographic and temporal heterogeneity, which provides more robust malaria data [10, 40, 44]. Expanding the study sample to include additional comparison countries magnified the association between PMI and coverage of ITNs, ACTs, and IRS, suggesting that access to malaria interventions in the 9 additional countries (Botswana, Central African Republic, Equatorial Guinea, Eritrea, Guinea-Bissau, Mauritania, Somalia,

South Sudan, and Sudan) was even more lacking than in the main study sample. The use of data spanning nearly 20 years enabled us to isolate the association between PMI and mortality from general shifts in child mortality trends in SSA and test the key assumptions of the difference-in-differences model. The finding that PMI and non-PMI countries had similar trends in child mortality rates prior to PMI introduction therefore strengthens the main finding regarding the association between PMI and child mortality rates. Lastly, PMI and comparison countries had similar governance characteristics when the program began, suggesting that it is unlikely that the program was selectively implemented in countries that were more favorable environments for malaria funding.

This study was subject to several limitations. First, difference-in-differences analysis relied on the assumption that there were no important unmeasured variables that differentially affected mortality rates in PMI and comparison countries during the study period. We used country fixed effects to control for all time-invariant differences between countries and year fixed effects to control for the underlying time trends in the region. Yet our study could still suffer from omission of important time-varying characteristics, which could bias our study results if the omitted variables affected PMI and comparison countries in different ways. For example, we were not able to account for national government spending on malaria interventions due to lack of reliable data. Countries have taken on more pronounced roles in funding their health systems and the potential contributions of domestic spending to the improved mortality rates should not be overlooked. Despite the increasing role of local governments globally, domestic malaria funding in SSA was fairly flat throughout the study period and, as of 2014, it still accounted for less than 10% of total malaria spending [1]. Nonetheless, PMI works in concert with recipient governments, and including national government contributions to fighting

malaria would provide a fuller picture of which models of delivering malaria interventions have the highest value for money. Given the ongoing debate about how foreign aid affects recipient governments' investments in the health sector [45-47], it is difficult to ascertain how governments might have adjusted their investment in malaria interventions after PMI was launched. This complicates the assessment of whether reallocation of resources was an important mechanism through which PMI was associated with all-cause mortality.

Second, the finding that Global Fund support was associated with only a modest reduction in all-cause child mortality, while consistent with one other study [48], should be interpreted with caution. The ability of our study to test hypotheses about the potential impact of this program was limited by the fact that all countries in our sample received Global Fund support by 2005. Thus, we did not have a comparison group of countries that did not receive Global Fund support, as we did for the evaluation of PMI. We suspect that the null finding can be largely explained by the lack of an appropriate comparison group that would have enabled us to test whether steady reductions in child mortality rates over time were due to Global Fund support or not. Our analysis of malaria interventions relied on the use of MAP data, which are modeled estimates. It is possible that the algorithm used to model the MAP data incorporated some inputs that were correlated with PMI. Finally, due to lack of suitable data, we were unable to evaluate whether the increase of IPTp (2 doses of sulfadoxine-pyrimethamine) coverage reported in PMI countries, from 14% at baseline to 38% in 2015 [8], are on par with or above the average trends in the rest of SSA. Future research should explore the potential impact of PMI on health behaviors in households with pregnant women.

### 2.5.3 Implications

Our findings provide important new evidence of an accelerated decline in child mortality rates after the introduction of PMI. The investments that PMI funding enabled in key malaria interventions was associated with a large reduction in all-cause under-5 mortality, higher coverage of ITNs and IRS, and modest increases in ACTs. Further investment in the interventions supported with PMI funds may translate to additional lives saved, reduced household financial burdens associated with caring for ill household members and lost wages, and less strain on health systems associated with treating malaria cases. In other words, the health gains from PMI investment may have spillover effects beyond health, such as higher school attainment and labor productivity, which might in turn lead to greater economic development. Future research should explore whether investments made through programs such as PMI did in fact improve education and economic outcomes in SSA. Improved capacity of health systems, whether through health systems strengthening or recipient countries' ability to shift their own resources to other health needs, might be a crucial component of PMI's success.

**Table 2.1. Description of study sample**

| Description of study sample | PMI countries | Comparison countries | Full sample |
|---|---|---|---|
| Description of under-5 mortality study sample (DHS data) | Frequency | Frequency | Frequency |
| Number of child-year observations | 5,837,998 | 1,914,073 | 7,752,071 |
| Child-year observations after PMI implementation | 1,266,884 | 0 | 1,266,884 |
| Child-year observations after Global Fund | 3,014,262 | 929,326 | 3,943,588 |
| Child-year observations after PEPFAR | 1,650,871 | 137,842 | 1,788,713 |
| Number of individual children in sample | 1,586,824 | 526,127 | 2,112,951 |
| Number of children under 5 years who died | 148,551 | 50,930 | 199,481 |
| Child mortality rate (per 1,000 person-years) | 25.4 | 26.6 | 25.7 |
| Description of malaria interventions coverage sample (MAP data) | | | |
| Number of country-year observations | 304 | 208 | 512 |
| Country-year observations after PMI implementation | 150 | 0 | 150 |
| Country-year observations after Global Fund | 243 | 160 | 403 |
| Country-year observations after PEPFAR | 143 | 43 | 186 |
| Number of individual countries in sample | 19 | 13 | 32 |

**Abbreviations**: DHS, Demographic and Health Surveys; MAP, Malaria Atlas Project; PEPFAR, President's Emergency Plan for AIDS Relief; PMI, President's Malaria Initiative.
**Notes:** PMI-recipient countries: Angola, Benin, Democratic Republic of Congo, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Tanzania, Uganda, Zambia, and Zimbabwe. Comparison countries: Burkina Faso, Burundi, Cameroon, Chad, Congo, Cote d'Ivoire, Gabon, Namibia, Niger, Sierra Leone, Swaziland, The Gambia, and Togo. **Notes**: Sample based on Demographic and Health Surveys from 32 sub-Saharan countries from 1995-2014. PMI recipient countries (year of implementation): Angola (2006), Benin (2008), Congo DRC (2011), Ethiopia (2008), Ghana (2008), Guinea (2011), Kenya (2008), Liberia (2008), Madagascar (2008), Malawi (2007), Mali (2008), Mozambique (2007), Nigeria (2011), Rwanda (2007), Senegal (2007), Tanzania (2006), Uganda (2006), Zambia (2008), Zimbabwe (2011). Comparison countries: Burkina Faso, Burundi, Cameroon, Chad, Congo, Cote d'Ivoire, Gabon, Namibia, Niger, Sierra Leone, Swaziland, The Gambia, and Togo.

**Table 2.2. Description of study countries**

| Description of countries in sample (MAP, WDI data) | PMI countries | Comparison countries | *p* value |
|---|---|---|---|
| Average *Plasmodium falciparum* rate in 2-10-year-olds in 2005, % | 30.0% | 30.2% | 0.980 |
| Under-5 mortality rate in 2005 (per 1,000 live births), mean | 121 | 128 | 0.541 |
| Population in 2005 (in thousands), mean | 28,713 | 7,790 | 0.030 |
| Adult literacy rate in 2005, % | 54 | 52 | 0.807 |
| GNI per capita in 2005 (PPP), mean | $1,466 | $4,015 | 0.052 |
| Health expenditures in 2005 (PPP), mean | 89 | 160 | 0.070 |
| Physician density in 2005 (per 1,000 people), mean | 0.10 | 0.11 | 0.680 |
| Nurse and midwife density in 2005 (per 1,000 people), mean | 0.66 | 1.45 | 0.108 |
| Government effectiveness index in 2005, mean[a] | −0.79 | −0.99 | 0.179 |
| Political stability index in 2005, mean[b] | −0.71 | −0.63 | 0.777 |
| Corruption index in 2005, mean[c] | −0.79 | −0.77 | 0.910 |

**Abbreviations:** %, Percent; GNI: Gross National Income; MAP, Malaria Atlas Project; PMI, President's Malaria Initiative; PPP, purchasing power parity (in 2011 constant dollars); WDI, World Development Indicators.

**Data Sources:** Average *Plasmodium falciparum* rate obtained from the MAP. Under-5 mortality rate, Population, Adult Literacy, GNI per capita, Health expenditures, Physician and Nurse density data obtained from the World Development Indicators, February 2017 version. Government effectiveness, Political stability and Corruption indexes obtained from The Worldwide Governance Indicators, 2015 Update.

[a] Government effectiveness reflects perceptions of the quality of public services, the quality of the civil service and the degree of its independence from political pressures, the quality of policy formulation and implementation, and the credibility of the government's commitment to such policies

[b] Political Stability measures perceptions of the likelihood of political instability and/or politically motivated violence, including terrorism.

[c] Corruption index reflects perceptions of the extent to which public power is exercised for private gain, including both petty and grand forms of corruption, as well as "capture" of the state by elites and private interests. Estimates of governance, corruption, and political stability range from approximately −2.5 (weak) to 2.5 (strong) performance.

**Table 2.3. Test of parallel trends assumption: risk of child mortality prior to PMI program implementation**

| Outcome | Annual risk of child mortality prior to PMI<br>RR [95% CI] |
|---|---|
| PMI-recipient country | 1.04 [0.96–1.13] |
| Linear time trend | 0.96*** [0.95–0.97] |
| PMI-recipient country * time interaction | 1.00 [0.98–1.01] |
| *Child's characteristics* | |
| Female | 0.89*** [0.87, 0.90] |
| Age (<1 year) | *Ref.* |
| Age (<2 years) | 1.64*** [1.51–1.79] |
| Age (<3 years) | 0.59*** [0.52–0.68] |
| Age (<4 years) | 0.41*** [0.37–0.45] |
| Age (<5 years) | 0.25*** [0.22–0.27] |
| *Mother's characteristics* | |
| No education | *Ref.* |
| Primary education | 0.89*** [0.86–0.93] |
| Secondary education | 0.77*** [0.74–0.80] |
| Higher education | 0.68*** [0.63–0.74] |
| Age | 0.94*** [0.93–0.94] |
| Parity | 1.18*** [1.17–1.19] |
| *Household characteristics* | |
| Rural residence | 1.09*** [1.05–1.14] |
| Lowest wealth quintile | *Ref.* |
| Second wealth quintile | 0.99 [0.94–1.04] |
| Middle wealth quintile | 0.95 [0.91–1.00] |
| Fourth wealth quintile | 0.88*** [0.82–0.95] |
| Highest wealth quintile | 0.71*** [0.67–0.75] |
| Female household head | 1.01 [0.99–1.03] |
| No. observations (children-years) | 6,174,926 |

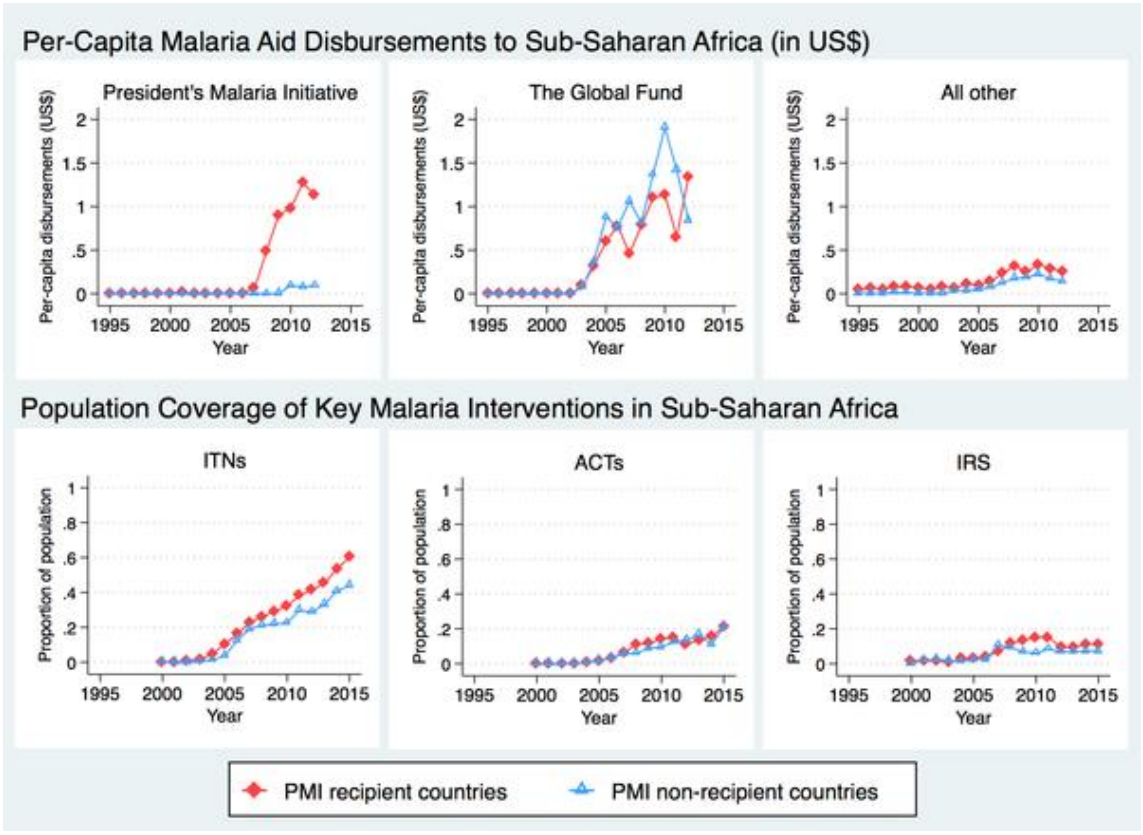
**Data Source:** Demographic and Health Surveys

**Abbreviations:** PMI, President's Malaria Initiative; RR, adjusted risk ratio

**Notes:** PMI-recipient country variable indicates whether a country eventually received PMI funds. Linear time trend measures secular mortality trends. The coefficient of interest is the interaction of PMI country indicator and linear time trend, which measures whether the mortality rates in countries that eventually received PMI differed from mortality trend in comparison countries, adjusted for individual-level covariates. Model also included country fixed effects. Standard errors were clustered at the country level. Sample excludes observations from PMI-recipient countries after the program was implemented.

: *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

**Figure 2.1. Time trends in development assistance for malaria and coverage of malaria interventions in sub-Saharan Africa**




Total assistance for malaria, in 2014 US dollars, was divided into 3 categories: (1) US bilateral aid for malaria, a proxy for PMI disbursements; (2) Global Fund, limited here to malaria disbursements; (3) All other malaria aid includes total malaria aid minus US bilateral aid minus GF malaria aid. **Data Sources:** Development Assistance for Health (DAH) data from 1995–2012 were obtained from Institute for Health Metrics and Evaluation. Population coverage of ITNs, ACTs, and IRS from 2000–2015 were obtained from the Malaria Atlas Project. **Abbreviations:** ACTs, estimated proportion of cases of fever in under-5 year olds that were treated with artemisinin combination therapy; IRS, estimated proportion of the population protected by indoor residual spraying of insecticides; ITNs, estimated proportion of people who slept under an insecticide-treated bednet on any given night; PMI, President's Malaria Initiative.

**Table 2.4. Association between PMI and annual risk of mortality among children <5 years in sub-Saharan Africa**

| Panel A: (binary measures of donors) | Annual risk of child mortality and binary program indicators | | |
|---|---|---|---|
| | (1) | (2) | (3) |
| | RR [95% CI] | RR [95% CI] | RR [95% CI] |
| Implemented program | | | |
| Post PMI implementation | 0.85** [0.74–0.96] | 0.84** [0.74–0.95] | 0.84** [0.74–0.96] |
| Post Global Fund implementation | | 0.95 [0.87–1.04] | 0.93 [0.85–1.02] |
| Post PEPFAR implementation | | 1.06 [0.96–1.17] | 1.05 [0.95–1.17] |
| No. observations (children-years) | 7,752,071 | 7,752,071 | 7,404,57 |
| Individual covariates | No | No | Yes |

| Panel B: (per-capita measures of donors) | Annual risk of child mortality and per-capita disbursements for health | | |
|---|---|---|---|
| | (4) | (5) | (6) |
| | RR [95% CI] | RR [95% CI] | RR [95% CI] |
| Per-capita aid disbursements (US$) | | | |
| PMI (US bilateral aid for malaria) | 0.84*** [0.77–0.90] | 0.85*** [0.78–0.92] | 0.86*** [0.79–0.93] |
| Global Fund (malaria only) | | 0.96* [0.93–1.00] | 0.96 [0.93–1.00] |
| Other aid for malaria | | 1.04 [0.89–1.21] | 1.04 [0.87–1.24] |
| Global Fund (HIV/AIDS and TB) | | 1.00 [0.96–1.03] | 1.00 [0.96–1.03] |
| PEPFAR (US bilateral aid for HIV/AIDS) | | 1.01 [0.99–1.02] | 1.01 [0.99–1.02] |
| All other disbursements for health | | 0.99 [0.98–1.01] | 1.00 [0.98–1.01] |
| No. observations (children-years) | 7,140,735 | 7,140,735 | 6,829,406 |
| Individual covariates | No | No | Yes |

**Data sources:** Demographic Health Surveys from 1995 to 2014; Development Assistance for Health Database from 1995 to 2012, and World Development Indicators. **Abbreviations**: PEPFAR, President's Emergency Plan for AIDS Relief; PMI, President's Malaria Initiative; RR, adjusted risk ratio; TB, tuberculosis.

**Notes:** Models (1) to (6) are briefly described in the Methods section and are described in detail in Appendix 1. All models included country and year fixed effects and were calculated using robust standard errors. Models (4)–(6) are limited to 1995–2012 because estimates for Development Assistance for Health Database were not available for later years. Models (3) and (6) included individual-level covariates: child's age and gender, mother's level of education, age and parity, rural/urban residence, household wealth and whether the head of household is female. The full list of individual-level estimates and confidence intervals is displayed in Tables D and E in Appendix 1. *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$.

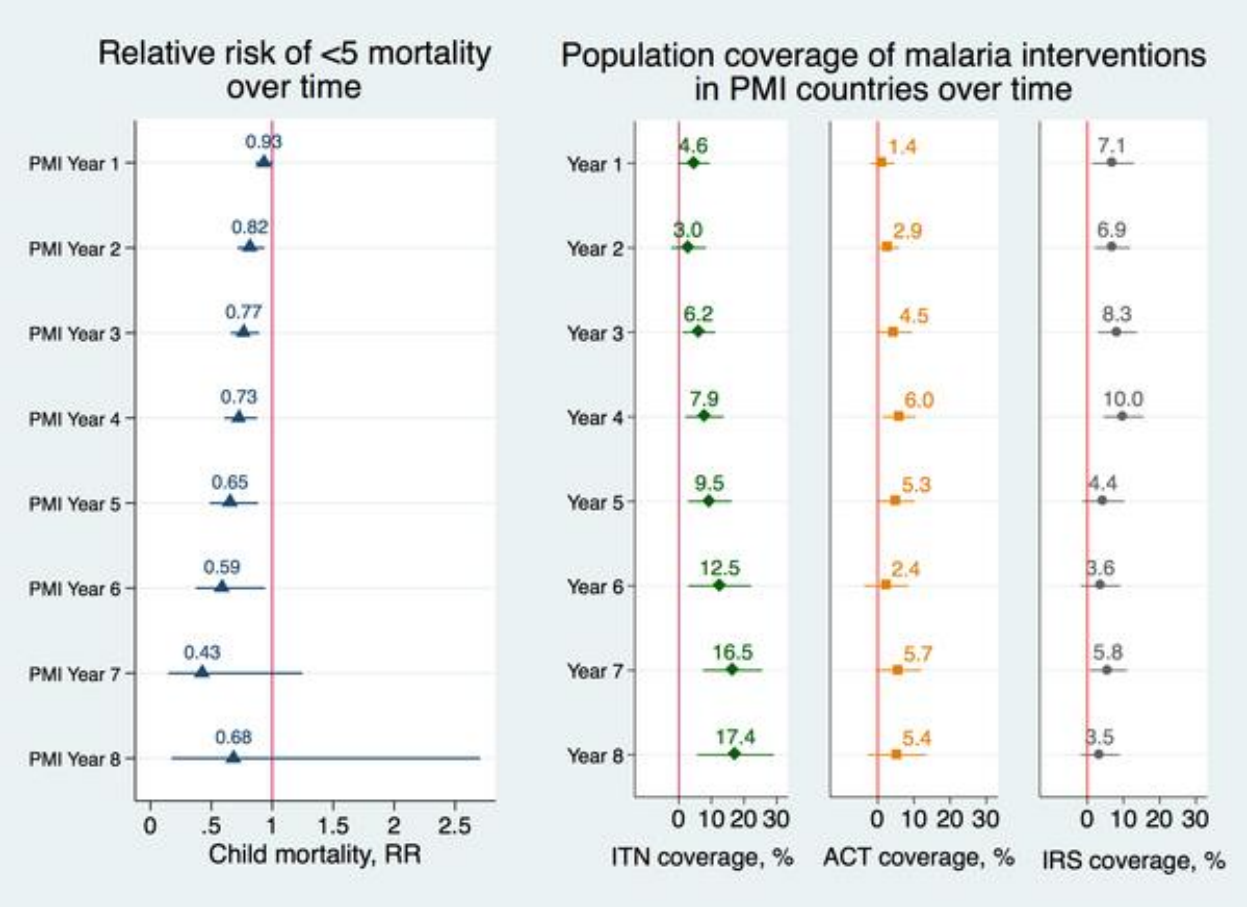
**Table 2.5. Population coverage of insecticide treated nets (ITNs), artemisinin-based combination therapy (ACTs), and indoor residual spraying (IRS) in 19 PMI-recipient countries compared to 13 non-recipient countries in sub-Saharan Africa**

| Panel A (binary measures of donors) | Models of population coverage of malaria interventions and program implementation | | |
|---|---|---|---|
| | ITNs (7) | ACTs (7) | IRS (7) |
| | Coef. [95% CI] | Coef. [95% CI] | Coef. [95% CI] |
| *Implemented program* | | | |
| Post PMI | 8.34* [0.86–15.83] | 2.98 [−3.18–9.14] | 6.63* [0.79–12.47] |
| Post Global Fund | −5.91 [−13.33–1.51] | 0.85 [−4.75–6.45] | 1.79 [−2.97–6.55] |
| Post PEPFAR | −3.23 [−11.27–4.82] | 1.30 [−3.02–5.62] | −1.06 [−4.88–2.77] |
| No. observations (country-years) | 512 | 512 | 512 |
| Average coverage in PMI countries before intervention | 7.0% | 1.1% | 3.0% |

| Panel B (per-capita measures of donors) | Models of population coverage of malaria interventions and per-capita disbursements for health | | |
|---|---|---|---|
| | ITNs (8) | ACTs (8) | IRS (8) |
| | Coef. [95% CI] | Coef. [95% CI] | Coef. [95% CI] |
| *Per capita aid disbursement (US$)* | | | |
| US bilateral aid for malaria | 4.29* [0.54–8.03] | 3.56 [−0.07–7.19] | 1.98 [−1.32–5.27] |
| Other aid for malaria | 9.69**[3.41–15.97] | 1.70 [−4.40–7.80] | 1.90 [−8.15–11.95] |
| Global Fund (malaria only) | 1.51 [−0.02 - 3.05] | 0.27 [−0.81–1.35] | 0.11 [−1.33–1.54] |
| Global Fund (HIV/AIDS and TB) | −0.22 [−0.77–0.34] | −0.12 [−0.38–0.15] | 0.61* [0.15–1.08] |
| US bilateral aid for HIV/AIDS | −0.39* [−0.73–−0.04] | −0.03 [−0.26–0.20] | −0.15 [−0.75–0.45] |
| All other disbursements for health | −0.39 [−1.18–0.39] | −0.15 [−0.74–0.44] | 0.16 [−0.48–0.79] |
| No. observations (country-years) | 416 | 416 | 416 |
| Average coverage in PMI countries before intervention | 7.0% | 1.1% | 3.0% |

**Data sources:** Malaria Atlas Project (MAP), Development Assistance for Health Database (DAH), and World Development Indicators (WDI).
**Abbreviations:** ACTs, estimated proportion of cases of fever in under-5 year olds that were treated with artemisinin combination therapy; Coef., coefficient; IRS, estimated proportion of the population protected by indoor residual spraying of insecticides ITNs, estimated proportion of people who slept under an insecticide-treated bednet on any given night; PEPFAR, President's Emergency Plan for AIDS Relief; PMI, President's Malaria Initiative; TB, tuberculosis.
**Notes**: Coefficients can be interpreted as percentage changes. All models also included country and year fixed effects and population size. Robust standard errors were used to calculate confidence intervals and *p* values. *** p<0.001, ** p<0.01, * p<0.05. Models (7) and (8) are briefly described in the Methods section and are described in detail in Appendix 1.

**Figure 2.2. Adjusted risk ratios of child mortality and adjusted percentage changes in population coverage of malaria interventions as a function of year of PMI program implementation**




Risk ratios of child mortality were estimated using modified Poisson regression model controlling for a set of indicators of the year of PEPFAR implementation, a set of indicators of the year of Global Fund implementation, individual-level covariates, country and year fixed effects (Model 9 in Appendix 1). Standard errors were clustered at the country level. Error bars represent 95% confidence intervals. Changes in ITN, ACT, and IRS coverage were obtained using OLS regression models, controlling for a set of indicators of the year of PEPFAR implementation, a set of indicators of the year of Global Fund implementation, individual-level covariates, country and year fixed effects (Model 10) and robust standard errors. PMI year 9 was omitted from the figure because too few observations were available for the calculations (full list of coefficients and confidence intervals is listed in Table G in Appendix 1). **Data Sources:** Demographic and Health Surveys from 1995–2014; Malaria Atlas Project from 2000–2014, Development Assistance for Health Database from 1995-2012 and World Development Indicators. **Abbreviations:** ACTs, estimated proportion of cases of fever in under-5 year olds that were treated with Artemisinin Combination Therapy; IRS, estimated proportion of the population protected; ITNs, estimated proportion of people who slept under an insecticide-treated bednet on any given night; PEPFAR, President's Emergency Plan for AIDS Relief PMI, President's Malaria Initiative; RR, risk ratio.

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# CHAPTER 3: HIGH CD4 COUNTS ASSOCIATED WITH BETTER ECONOMIC OUTCOMES FOR HIV-POSITIVE ADULTS AND THEIR HIV-NEGATIVE HOUSEHOLD MEMBERS IN THE SEARCH TRIAL

## 3.1 Overview

**Background:** Country decisions to scale-up "test-and-treat" approaches for HIV depend on consideration of both the heath and economic consequences of such investments. Evidence about economic impact of expanded ART is also relevant for decisions regarding foreign assistance for HIV/AIDS programs, which are facing proposed cuts by the U.S. government. We used baseline data from the Sustainable East Africa Research in Community Health (SEARCH) cluster randomized controlled trial in rural Uganda and Kenya to examine the association between HIV status, CD4+ T-cell counts, viral suppression, and multiple indications of economic well-being.

**Methods and Findings:** Socio-economic surveys were conducted in households with HIV-positive and HIV-negative adults sampled after census from each of the 32 communities participating in the SEARCH trial (NCT01864603). Cross-sectional data were obtained for 11,588 individuals from 5,944 households in the study communities. Participants were stratified based on their own HIV status as well as CD4 cell counts and viral suppression status if they were HIV-positive. HIV-negative participants residing in households with no HIV-positive adults were considered separately from HIV-negative participants residing in households with ≥1 HIV-positive adult. Generalized estimating equation models were used to examine the relationship between HIV status, CD4 counts, antiretroviral therapy (ART), viral suppression, and outcomes of employment, self-reported illness, healthcare utilization, and health

expenditures. In all models, HIV-negative participants in households with no HIV-positive persons were the reference group.

No significant difference was observed in the likelihood of being employed between HIV-positive participants with CD4>500 (i.e. the healthiest HIV-positive individuals) and the reference group (AOR 1.10, 95% CI 0.93-1.29). However, HIV-positive participants with CD4≤350 (i.e. the least healthy individuals) were less likely to be employed than the reference group (adjusted odds ratio, AOR, 0.66, 95% CI 0.54-0.80), as were HIV-positive participants with CD4 351-500 (i.e. individuals whose health status began to decline, AOR 0.77, 95% CI 0.63-0.94). Similarly, there was no significant difference in employment outcomes between HIV-negative participants who resided in households with a CD4>500 HIV-positive person and the reference group (AOR 0.91, 95% CI 0.75-1.10). HIV-negative participants residing with an HIV-positive person with CD4≤350, however, were less likely to be employed than the reference group (AOR 0.71, 95% CI 0.56-0.90), as were people residing with a household member with CD4 351-500 (AOR 0.68, 95% CI 0.54-0.86). HIV-positive participants in all CD4 categories were more likely than the reference group of HIV-negative participants to have lost time from usual activities due to illness and have incurred healthcare expenditures. HIV-positive participants with CD4>500 had better employment outcomes than those with CD4 351-500, even among those who were not virally suppressed ($p$=0.004) and not on ART ($p$=0.01).

**Conclusions:** Data from a large population-representative sample of households in rural Kenya and Uganda showed a strong negative association between poor health status of HIV-positive persons and several economic outcomes. The findings suggest substantial economic benefits may be associated with maintaining high CD4 counts, for both HIV-positive persons and their HIV-negative household members. This association is consistent with the hypothesis that

early ART initiation can avert declines in employment and other economic outcomes. Ongoing prospective longitudinal evaluation is needed to further assess the full economic impacts of early ART initiation, including test-and-treat strategies.

### 3.2 Background

Compelling evidence on the public health benefits of antiretroviral (ART) treatment as prevention and the individual-level benefits of early ART initiation [1, 2] was the foundation for the 2015 WHO guidelines that recommend treatment for all persons living with HIV and the UNAIDS 90-90-90 targets, which call for 90% of people living with HIV to know their status, 90% of HIV-positive people to receive ART, and 90% of people on ART to reach viral suppression by 2020 [3, 4]. Despite these data and recommendations, less than half of countries have adopted the WHO guidelines, and the pace of implementation is threatened even among countries moving forward to HIV "test-and-treat" [5]. A number of factors contribute to this delay, but arguably, the biggest challenge is that even in the face of the strong public health case and predictions from economic models, many countries remain concerned about the required investment [3, 6-8]. Growing uncertainty about continued levels of support from the US government for HIV/AIDS programs through the President's Emergency Plan For AIDS Relief (PEPFAR) and other initiatives [9] that could put an even greater financial burden on low-income countries that depend on this financing. Policymakers could benefit from assessments of potential economic gains of finding and keeping HIV-positive persons in the high CD4+ range through early ART initiation—gains that may be realized by the affected HIV-positive individual and their households.

Longitudinal studies conducted in sub-Saharan Africa (SSA) during the past decade show that ART initiation among individuals with low CD4+ T-cell counts, in line with prior WHO guidelines, leads to dramatically improved individual- and household-level economic outcomes

[10-17]. These studies report sustained improvements in outcomes ranging from labor force participation, income, and quality of life for the individuals receiving ART. A limited number of additional studies have also documented benefits to household members of treated adults, particularly in the form of reduced domestic labor burden [18] and increased school enrollment for children [19]. One study showed that ART expansion led to increased work hours of HIV-negative people whose households did not directly benefit from the treatment [20]. Although these studies offer persuasive evidence of the economic recovery following ART initiation for those with low CD4 counts, no study to date has assessed whether ART initiation among asymptomatic patients with high CD4 counts also generates economic benefits. Crucial to the discussion of economic benefits of test-and-treat is the hypothesis that delayed ART initiation may lead to a period of health and economic decline along with incomplete recovery even when patients adhere to ART. Thus, averting a decline of outcomes through early ART initiation may offer important benefits that extend beyond the health sector.

Although a positive association between employment outcomes and CD4 counts has been documented in a rural Ugandan setting [21], data from a larger population on a wider set of indicators of economic well-being are lacking. Also, information on viral loads of HIV-positive persons has seldom been integrated into analyses. Because most studies have focused on outcomes of patients initiating ART, less is also known about how HIV-negative household members fare when an HIV-positive household member has high vs. low CD4 counts. This study utilizes data collected after baseline census and population-level HIV testing in a large community cluster randomized trial conducted in two countries, Kenya and Uganda, to examine the association between HIV status, CD4 counts, viral suppression and ART status of all adult household members, and multiple indications of economic well-being.

## 3.3 Methods

### 3.3.1 Study procedures

Data were collected in 32 rural communities participating in the ongoing Sustainable East Africa Research in Community Health (SEARCH) HIV test-and-treat cluster randomized controlled trial (NCT01864603). The trial procedures are described in detail elsewhere [22]. Briefly, study communities consisting of approximately 10,000 individuals each are in three distinct geographic regions with varying HIV prevalence; 12 communities are in western Kenya, 10 in eastern Uganda, and 10 in southwestern Uganda. At the beginning of the trial (baseline), a door-to-door census was conducted in each community and followed by 2-week multi-disease community health campaigns (CHCs) that included HIV testing, counselling, and referral to care for HIV-positive persons. Individuals aged >10 years who participated in census but did not attend the CHCs were subsequently approached for home-based testing. This "hybrid" testing approach was found to achieve 89% population-level HIV testing coverage [22].

Following the CHCs and in parallel with home-based testing, a random sample of households with and without an HIV-positive adult were selected for structured household surveys that were administered to adults in the household. In each SEARCH community, we conducted surveys with 100 households that included an HIV-positive adult and 100 households that did not include an HIV-positive adult. The household surveys sought to assess socio-economic conditions of households and individuals residing in them. Several survey sections obtained information on individuals' demographic characteristics, employment and income of household members aged ≥12 years, ownership of durable goods and livestock, health care utilization, and education of household members aged 6-25 years. Reports were obtained for all household members from one person, typically the household head or spouse of household head. These surveys were adapted from The World Bank's Living Standards Measurement Surveys

that have been administered to households in many low- and middle-income countries [23]. Survey questionnaires were administered by trained research assistants who visited homes of selected participants. Information collected in the household surveys was linked at the individual level to SEARCH data on HIV status, and for HIV-positive individuals, their CD4 count.

### 3.3.2 Ethics statement

The Makerere University School of Medicine Research and Ethics Committee (Uganda), the Ugandan National Council for Science and Technology (Uganda), the Kenya Medical Research Institute Scientific Ethics Review Unit (Kenya), and the University of California San Francisco Committee on Human Research (USA) approved the consent procedures and the study. All participants provided verbal informed consent in their preferred language with a signature or fingerprint confirmation of consent.

### 3.3.3 Outcome measures

Questionnaires assessed several aspects of baseline employment and healthcare utilization among survey respondents and their household members. Participation in the labor force was assessed with a binary indicator of whether an individual spent any time working (both on- or off-farm) in the week prior to the survey. Total number of hours worked on and off farm was also obtained, censoring outlier values at the $95^{th}$ percentile. Since most households were primarily engaged in subsistence agriculture, we separately evaluated participation in the agriculture sector with a binary indicator of whether an individual did farm work in the past week. Health status of the study participant was measured using a binary indicator of any illness episodes in the past month. An illness episode included any type of illness or injury, for example cough, cold, diarrhea, or injury due to an accident. The potential economic burden of illness was measured with an indicator of whether the participant lost time from usual activities (employment and domestic activities) due to illness in the past month. Healthcare utilization was

measured as a binary indicator of any care sought or received last month, any health expenditures last month, and any hospitalizations in the past year. Healthcare expenditures included travel for medical care costs, inpatient and outpatient fees, medicines, laboratories and other healthcare costs. The recall period for hospitalization was one year prior given the rarity of such events. Number of hours lost from usual activities due to illness, number of hours spent seeking or receiving care, and amount of health expenditures, in 2014 US dollars, were also obtained from study participants, with outlying values censored at 95$^{th}$ percentile.

### 3.3.4 Laboratory-confirmed indicators

HIV status of individuals was determined by rapid HIV tests obtained in the hybrid testing approach, i.e. CHCs and home-based testing. Laboratory-confirmed CD4+ T-cell count/mL measured at baseline CHCs and home-based testing were used to characterize HIV-positive participants' disease stages [22]. HIV RNA levels were measured as previously described [24]; viral suppression was defined by RNA levels <500 copies/mL. Finally, we used ART start date, based on information extracted from Ministry of Health data and study records, to determine whether HIV-positive participants initiated ART at least 1 month prior to the household survey.

### 3.3.5 Statistical analyses

We conducted two sets of complementary analyses. First, we focused on HIV-positive persons and sought to understand the association between HIV status, HIV disease progression, and socio-economic outcomes. We compared outcomes of HIV-positive participants grouped by their CD4 counts to outcomes of HIV-negative participants in households without an HIV-positive person (a group of individuals that would be least-affected by HIV/AIDS). HIV-positive participants were grouped by their CD4 counts in three categories that reflect various thresholds used for ART initiation: ≤350 cells/μL, 351-500 cells/μL, and >500 cells/μL. Second, we focused

on HIV-negative persons and sought to examine the association between having an HIV-positive household member and various socio-economic outcomes. We therefore compared outcomes of HIV-negative participants grouped by their HIV-positive household members' CD4 counts to the outcomes of HIV-negative participants in households without any HIV-positive person. HIV-negative participants in households with an HIV-positive person were grouped based on the HIV-positive person's CD4 count. In cases where a household had ≥2 HIV-positive persons, the lowest CD4 count was used to categorize participants. In all models, HIV-negative participants who lived in households without any HIV-positive person served as the reference group.

We used generalized estimating equations (GEE) regression models to analyze the binary dependent variables as a function of HIV status and HIV disease stages, defined by the laboratory-confirmed CD4 T-cell counts. We fitted GEE models using binomial distribution, logistic link, and exchangeable correlation at the household level [25]. We set significance level at alpha=0.05. Models controlled for ART status, age, age-squared (to capture non-linear effects of age), education (indicators for no education, some primary education, completed primary education, some secondary education, and completed secondary education or greater), gender (indicator for female), marital status (indicator for married or cohabiting), wealth index (in quintiles), number of children in household, and household size. Community indicators were also included to control for underlying differences between the communities. The wealth index was calculated using the first component of a principal component analysis of ownership indicators of 47 different household items [26]. We restricted the analytic sample to individuals who had non-missing data for all outcomes and explanatory variables of interest. Post estimation Wald tests were used to perform two-sided hypothesis tests about equality of the CD4>500 coefficient

to the CD4≤350 and CD4 351-500 coefficients (and the equivalent of HIV-negative participant groups based on HIV-positive household members' CD4 counts).

Finally, we tested whether there was an association between CD4 counts and economic outcomes among HIV-positive participants using their ART initiation status and detectable viral load status. This GEE estimation categorized HIV-positive participants in the 3 CD4 groups by whether or not they were receiving ART and whether or not they were virally suppressed. High CD4 participants who were virally suppressed were assumed to have achieved recovery in health status through ART. High CD4 participants who were not virally suppressed included newly infected HIV participants identified through the comprehensive SEARCH testing strategy, as described above, and patients who have been on ART but have not reached viral suppression. We also performed Wald tests to determine whether the association for those with CD4>500 not on ART was the same as for those with CD4>500 on ART and CD4 351-500 CD4 not on ART. Similar tests were performed with the viral suppression indicators.

Lastly, we used nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing) [27] to visually examine the association between CD4 counts and the continuous outcomes: the number of hours worked, number of hours lost from work due to illness, number of hours spent seeking healthcare, and healthcare expenditures. We compared the nonparametric results using linear regression models that adjusted for the same set of covariates as the GEE models.

## 3.4 Results

### 3.4.1 Study participants

Data were collected between July 2013 and August 2014 for 34,029 individuals living in 6,309 households. This sample represented 10.2% of the 335,024 residents in the SEARCH trial communities at baseline. We limited our analytic sample to working-age adults, defined as those aged 18-65 years (n=14,449) whose HIV status was known (n=11,873) and whose CD4 laboratory results were available if HIV-positive (n=11,705). The final analytic sample was further restricted to participants who had non-missing data on outcomes and explanatory variables (n=11,588 from 5,944 households).

Table 3.1 summarizes outcomes and other descriptive characteristics of the working-age adults in our sample with non-missing data. By design, nearly half the sample (48%) consisted of HIV-negative participants in households with no HIV-positive persons. Twenty-one percent of participants were HIV-negative and lived in households with ≥1 HIV-positive person. Approximately 31% of all participants (n=3,626) were HIV-positive, and 50% (n=1,798) of those individuals had CD4>500, 24% (n=887) had CD4 351-500, and 26% (n=939) had CD4≤350.

Over half the participants (56%) had completed less than primary education, with HIV-negative individuals having higher education and slightly higher household wealth. The majority of participants were active in the labor force in the past week, with 70% and 58% of all participants reporting having done any work or farm work, respectively. Labor force participation rates were lowest for HIV-negative participants in households with ≥1 HIV-positive person. Approximately one-third of all participants reported an illness in the past month and nearly one-fifth of all participants reported having sought or received healthcare in the past month, having lost time from usual activities due to illness, and having spent money on treatment

in the past month. Hospitalization in the past year was reported by 7% of all participants, with HIV-positive participants being most likely to be hospitalized. Overall, HIV-positive participants reported more illness and higher healthcare expenditures. The average age among participants was 35 years and nearly 58% were women.

### 3.4.2 Regression results

Figure 3.1 displays the results of nonparametric regressions that estimated the unadjusted association between CD4 counts and four continuous measures of employment and healthcare-related outcomes among HIV-positive adults. HIV-positive adults with higher CD4 counts worked more hours, lost fewer hours from usual activities due to illness, spent fewer hours seeking healthcare, and spent less money on healthcare. These patterns were also found in adjusted regression models (Appendix 1).

Results in Table 3.2 show that the health status of HIV-positive participants, as indicated by CD4 counts, was associated with employment outcomes. Compared to the reference group of HIV-negative participants in households with no HIV-positive person, HIV-positive participants with CD4≤350 were less likely to have worked in the past week (adjusted odd ratio, AOR, 0.66, 95% CI 0.54-0.80), as were those with CD4 351-500 (AOR 0.77, 95% CI 0.63-0.94). HIV-positive participants with CD4>500, on the other hand, had equal odds of working in the past week as the reference group (AOR, 1.10, 95% CI, 0.93-1.29). Post-estimation Wald tests showed HIV-positive participants with CD4>500 were more likely to have worked than those with CD4 351-500 and CD4 ≤350 ($p$<0.001 in both tests). We found largely similar patterns in farm work as well, with HIV-positive participants with high CD4 counts being similar to the reference group and those with low CD4 counts less likely to be doing farm work. Being on ART was associated with higher odds of having done any work in the past week (AOR 1.23, 95% CI 1.03-1.45) as well as any farm work (AOR 1.25, 95% CI 1.08-1.45).

For HIV-negative participants, those residing in households with an HIV-positive person who had low CD4 counts (≤350 or 351-500) were less likely to be engaged in the labor force than the reference group (Table 3.3). For example, those in households with an HIV-positive person with CD4≤350 had 0.71 lower odds of having worked in the past week (95% CI 0.56-0.90) and 0.80 lower odds of farm work in the past week (95% CI 0.64-1.00). In contrast, HIV-negative participants in household with an HIV-positive person with CD4>500 had statistically equal odds of working (AOR 0.91, 95% CI 0.75-1.10) as their counterparts in households with no HIV-positive persons. Post-estimation Wald tests showed that odds of any work and farm work last week were statistically higher for individuals whose household members had >500 CD4 counts than individuals who lived with HIV-positive participants with CD4 351-500 ($p$=0.023 and $p$=0.016, respectively).

HIV-positive individuals in all CD4 categories were significantly more likely to have experienced illness, lost time from usual activities due to illness, sought healthcare and spent money on healthcare than HIV-negative participants in households with no HIV-negative persons (Table 3.4). For example, compared to the reference group, odds of seeking healthcare in the past month were much higher for HIV-positive participants with CD4≤350 (AOR 1.78, 95% CI 1.48-2.13), CD4 between 351-500 (AOR 1.67, 95% CI 1.38-2.01), and CD4>500 (AOR 1.31, 95% CI 1.12–1.53). Participants with CD4≤350 had more than two times the odds of hospitalization in the past year than the reference group (AOR 2.32, 95% CI 1.79-3.02) and their odds of hospitalizations much higher than for individuals with CD4 351-500 ($p$=0.051). Participants with CD4 counts in the 351-500 range also had higher odds of hospitalizations last year compared to HIV-negative participants (AOR 1.74, 95% CI 1.32-2.30) as did individuals

with CD4>500 (AOR 1.37, 95% CI 1.09–1.73). In all the analyses, HIV-positive participants with CD4>500 fared better than individuals with CD4≤500, as indicated by post-estimation tests.

HIV-negative participants who lived with HIV-positive household members were less likely to experience illness, lose time from usual activities due to own illness or care-seeking, and spend money on healthcare than their counterparts in households without an HIV-positive person (Table 3.5). For example, HIV-negative participants whose household members had CD4 counts in the 351-500 range were less likely to have experienced illness (AOR 0.75, 95% CI 0.58-0.96), lost time from activities due to illness in the past month (AOR 0.68, 95% CI 0.50-0.92), sought or received healthcare in the past month (AOR 0.75, 95% CI 0.55-1.02), or spent money on healthcare (AOR 0.72, 95% CI 0.53-0.98).

Finally, high CD4 participants (>500) not on ART had statistically equal outcomes as HIV-negative participants (Table 3.6, Panel A: AOR for employment 1.11, 95% CI 0.93-1.32; AOR for healthcare expenditures 1.17, 95% CI 0.98-1.39). HIV-positive participants with CD4≤500 and not on ART had significantly worse outcomes than HIV-negative participants (AOR for employment 0.75, 95% CI 0.59-0.95; AOR for healthcare expenditures 1.69, 95% CI 1.34-2.11) and HIV-positive participants with high CD4 and not on ART ($p$=0.004 for employment and $p$=0.006 for healthcare expenditures). HIV-positive participants on ART with recovery to CD4>500 reported economic losses due to illness that were higher compared to both HIV-negative and newly identified HIV-positive participants with high CD4. When participants were stratified based on viral load suppression (Table 3.6, Panel B), we largely found the same associations. Participants with high CD4 and detectable viral loads had similar economic outcomes to HIV-negative participants, but participants with high CD4 and undetectable viral

load were significantly more likely to lose time from usual activities due to illness and to have accrued health expenditures due to illness.

### 3.5 Discussion

In this large, population-representative study from 32 communities participating in the SEARCH trial in Kenya and Uganda, economic outcomes for HIV-positive individuals with high CD4+ T-cell counts (>500) were significantly better than those for HIV-positive individuals with CD4≤500 and were comparable to outcomes for HIV-negative participants. For HIV-negative household members of HIV-positive persons, the CD4 counts of the HIV-positive household member was similarly protective of employment outcomes. Patterns in healthcare utilization and healthcare costs incurred by HIV-positive individuals also indicated a benefit to having higher CD4 counts, even though the outcomes of those with CD4>500 remained poorer than those for HIV-negative persons in households not directly affected by HIV. Importantly, even among HIV-positive participants who had not initiated ART or were not virally suppressed, those with CD4>500 had better economic outcomes than those with lower CD4 counts, including in the range of 351-500 cells/μL. These findings suggest that initiating ART before CD4 counts decline below 500 could generate economic benefits, though the results need to be confirmed in future analyses using longitudinal data.

Unlike many prior studies of adults initiating ART and population-based studies, many of which lack data on key health indicators such as the CD4 count and HIV RNA and are based on samples of HIV-positive people whose health status declined as they awaited treatment initiation [10-17, 21, 28], this study offers a depiction of the association between CD4 counts and economic outcomes in the general population. Although previous studies have documented an individual-level decline in employment outcomes in the years prior to ART initiation at CD4<200, followed by a rebound in economic outcomes following ART initiation at the low

CD4 counts, studies that assess outcomes of asymptomatic, high CD4 adults are lacking. In this cross-sectional study, several economic outcomes of HIV-positive, high CD4 individuals were assessed and contrasted to those of other HIV-positive and HIV-negative individuals. By and large, the findings from this study are consistent with the hypothesis that population level HIV testing and early ART initiation may help avert an economic decline associated with HIV disease progression.

Previous studies document that early ART initiation offers important individual health benefits and reduces the risk of HIV transmission [1, 2]. This study's findings provide policymakers with additional data on the potential economic gains of finding and treating persons with HIV early in their disease course. It is particularly noteworthy that HIV-positive adults with CD4>500 generally had significantly higher employment rates than even those with CD4 cell counts between 351-500. Although further evidence from longitudinal assessments based on controlled trials would be useful, this association is suggestive of an economic benefit to ART initiation at CD4>500. The associations that were quantified in this study also suggest that the benefits of early ART initiation may be sizable when it comes to outcomes such as employment and healthcare utilization, as high CD4 individuals generally had significantly higher odds of employment and lower healthcare burdens than low CD4 individuals.

To our knowledge, this study provides the first assessment of economic outcomes of HIV-positive individuals over a wide range of disease stages as well as the socio-economic outcomes of their household members. Access to laboratory-confirmed HIV status and CD4 counts allowed us to determine the health status of study participants using objective measures, and the design of the household survey provided measures of a wide range of economic outcomes. Some results from this study confirmed and extended previous findings about the

associations between severity of HIV disease, ART, and employment outcomes. Consistent with existing literature, we found that HIV-positive individuals on ART had better economic outcomes [10, 12, 18, 21, 28]. The findings for individuals with CD4 counts >500 also confirmed, with greater precision, the results from a small pilot study that our team conducted in one community in southwestern Uganda [21].

This study is also noteworthy for its analysis of how HIV-negative household members may be associated with the health status on an HIV-positive person. The findings illustrate several potential "spillover effects" of HIV disease progression on economic functioning of HIV-negative household members. In households where HIV-positive adults had high CD4 counts, HIV-negative household members typically had similar employment outcomes as HIV-negative individuals in households without an HIV-positive person. On the other hand, residing with HIV-positive adults who had CD4≤500 was associated with worse economic outcomes. This finding suggests that maintaining high CD4 counts can have population-level economic impacts that are greater than those among HIV-positive persons alone, a hypothesis that needs to be tested using longitudinal data. Consistent with this possibility, it is notable that a recent study showed that the introduction of PEPFAR in SSA, which led to many HIV-positive persons with low CD4 counts initiating ART, was associated with improved population-level employment outcomes [17]. Another study found proximity to ART increased work hours of HIV-negative people whose households did not directly benefit from expanded treatment [20]. Our cross-sectional study adds to the evidence indicating that ART may have "spillover effects" that extend beyond the HIV-positive persons receiving treatment.

Our findings have greater relevance given the recent focus on achieving 90-90-90 targets through greatly expanded HIV testing and access to ART, the emphasis on the need for increased

resources to achieve these targets [6], as well as the accompanying concern that development assistance for health has stagnated and that future funding levels are uncertain [29]. The combination of increased demands on countries to finance their own programs and the proposed cuts to U.S. foreign assistance [9] could undermine the prospects of achieving the 90-90-90 targets in countries that are most affected by HIV/AIDS. Furthermore, questions have been raised by the new U.S. administration about the value of large humanitarian aid programs such as PEPFAR [30]. Along with a series of other economic studies, this study provides compelling evidence of the economic and health system benefits that are associated with protecting and improving the health outcomes of HIV-positive persons and, therefore, the potential value of investing in global health programs such as PEPFAR. The evidence presented in this study can also be useful for governments of low-income countries for priority-setting in their own budgets, including allocation of resources towards health programs.

Important yet seldom measured costs of HIV infections are the indirect costs associated with ART. Despite ART drugs being offered free of charge to eligible patients in SSA, studies have documented significant costs associated with being on ART, including drugs to treat opportunistic infections or comorbidities, non-routine laboratory tests, medical consultations, and hospital stays [31-33]. This study's findings suggest that in households faced with high costs of care and treatment for one HIV-positive person, other household members may forgo some of their routine healthcare needs. This finding could have important future repercussions if untreated diseases of HIV-negative individuals lead to worsening symptoms, costlier treatment, and exit from the labor market. Thus, early access to ART may offer important benefits at the population level in the long term. Future cost-effectiveness studies should consider incorporating in their models the broader spillover effects of early ART once causal evidence from longitudinal

studies emerges rather than relying solely on the individual costs and benefits for the treated person [7].

Our study has several limitations. First, we were not able to establish causality of health status on economic outcomes using cross-sectional data. Follow-up longitudinal data collection in the SEARCH trial is ongoing, and we will be able to estimate the causal effect of early ART initiation on various economic outcomes once these data are collected. Second, many outcome measures were obtained in household surveys and could have suffered from recall bias. We attempted to limit these biases by using short recall periods that are common in similar literature [34]. Moreover, the main indicators of the health status of individual persons were laboratory-confirmed measures of HIV status and CD4 counts. The use of objective measures of health status represents an advance in comparison to other studies of the link between health and economic outcomes that relied on self-reported health status [35]. Third, the measure of ART status was based on treatment initiation dates rather than adherence, which could have led to misclassification of some people as being on ART (and therefore having better health) even if they did not have high adherence. For this reason, our estimates of the association between ART status and economic outcomes may be biased toward the null. Finally, the employment outcomes we relied on in this study were measures of labor market participation rather than productivity. Future studies should incorporate more robust measures of labor productivity (e.g. amount of income earned per day of work) to improve our understanding of how HIV impacts the earning potential of people living with the disease.

At a time where countries most affected by the HIV epidemic are faced with increasing financial challenges to fund the HIV response, our study provides evidence about the potential economic benefits of earlier ART initiation. While we cannot draw causal conclusions using

cross-sectional data, our findings provide important insights about the associations between the CD4 counts and ART use of HIV-positive persons and the economic outcomes they and their HIV-negative household members achieve. Future data from the SEARCH trial will enable us to test the hypothesis that early ART initiation has a causal effect on individual- and household-level economic outcomes.

**Table 3.1. Descriptive characteristics of study participants**

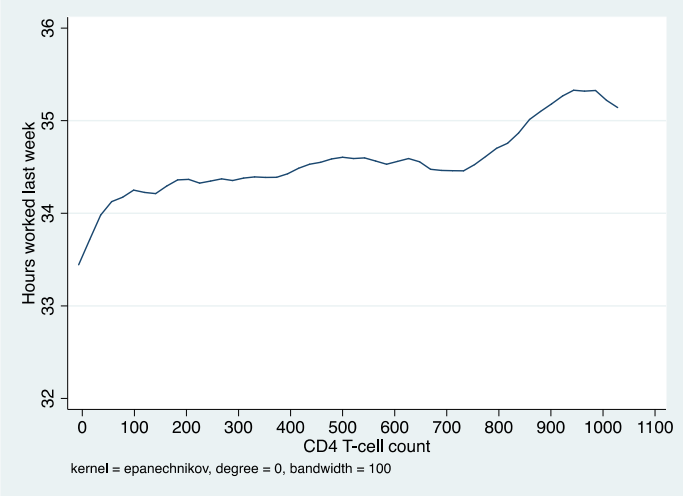
| | Study Group | | | | | |
|---|---|---|---|---|---|---|
| | HIV-, no HIV+ household members | HIV-, lives with HIV+ household members | HIV+ CD4 ≤350 | HIV+ CD4 351-500 | HIV+ CD4 >500 | Full Sample |
| No. individuals in study group | 5,556 | 2,406 | 941 | 887 | 1,798 | 11,588 |
| Percent of full sample in study group | 47.9 | 20.8 | 8.1 | 7.7 | 15.5 | 100 |
| ***Study outcomes*** | | | | | | |
| Worked last week, % | 70.9 | 59.1 | 74.3 | 75.8 | 79.2 | 70.4 |
| Worked on a farm last week, % | 58.7 | 49.4 | 57.4 | 62.3 | 63.1 | 57.7 |
| Experienced illness last month, % | 28.2 | 22.2 | 43.6 | 42.6 | 37.3 | 30.7 |
| Lost time from usual employment or household activities due to illness last month, % | 17.1 | 12.8 | 28.7 | 27.2 | 24.1 | 19.0 |
| Sought or received care last month, % | 16.7 | 13.5 | 31.3 | 30.0 | 25.6 | 19.6 |
| Spent money on healthcare last month, % | 17.3 | 13.9 | 29.4 | 29.8 | 24.9 | 19.7 |
| Hospitalized last year, % | 5.6 | 4.7 | 13.5 | 10.9 | 9.3 | 7.0 |
| ***Descriptive characteristics*** | | | | | | |
| Enrolled in ART, % | 0.0 | 0.0 | 49.4 | 47.2 | 42.6 | 14.2 |
| Age, mean | 34.3 | 32.1 | 39.2 | 38.5 | 36.2 | 34.9 |
| Female, % | 55.8 | 52.0 | 53.0 | 60.3 | 73.9 | 57.9 |
| Married or cohabiting, % | 68.4 | 53.9 | 69.0 | 67.8 | 67.7 | 65.3 |
| No education, % | 13.0 | 12.3 | 13.9 | 13.9 | 14.7 | 13.3 |
| Some primary education, % | 41.5 | 38.8 | 45.1 | 47.9 | 47.6 | 42.7 |
| Completed primary, % | 16.6 | 14.7 | 20.0 | 18.7 | 18.8 | 17.0 |
| Some secondary, % | 18.1 | 23.0 | 13.6 | 13.5 | 13.1 | 17.6 |
| Completed secondary or higher, % | 10.8 | 11.1 | 7.4 | 6.0 | 5.8 | 9.5 |
| Wealth quintile, mean | 3.2 | 3.3 | 3.0 | 2.9 | 3.0 | 3.2 |
| Number of children, mean | 3.5 | 3.5 | 2.9 | 2.9 | 3.0 | 3.3 |
| Household size, mean | 6.5 | 7.1 | 5.4 | 5.3 | 5.4 | 6.3 |

**Abbreviations:** No., Number; %, Percent; HIV+, HIV-positive; HIV-, HIV-negative; ART, antiretroviral therapy

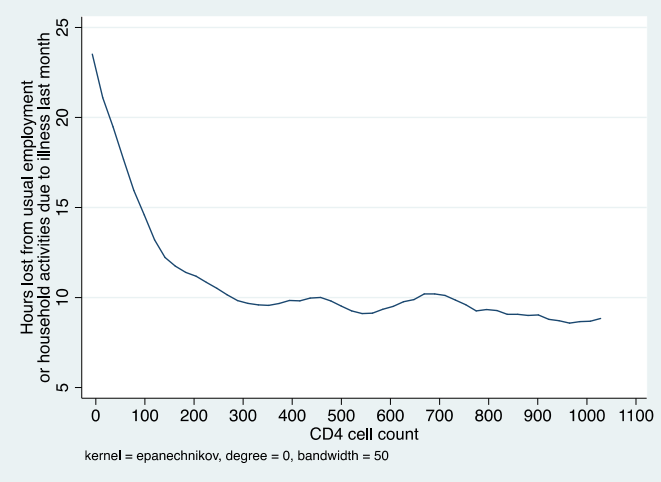
**Notes:** HIV-negative participants are stratified based on whether they resided with HIV-positive household member. Antiretroviral therapy status at baseline was established using first medication pickup date. Participants were defined as being enrolled in ART if their first ART pickup date was before the CHC campaign began in their community. Wealth, in quintiles, was calculated using Principal Components Analysis and was based on ownership of 47 items.

**Figure 3.1. Local polynomial graphs of employment and healthcare outcomes and CD4 counts among HIV-positive adults**

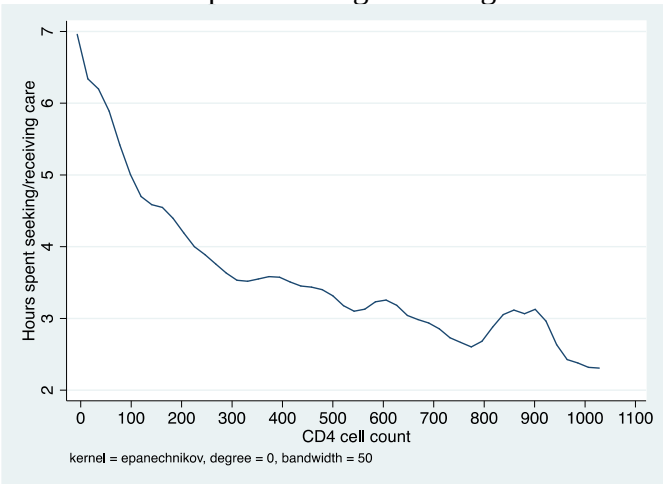
Panel A. Total hours worked last week



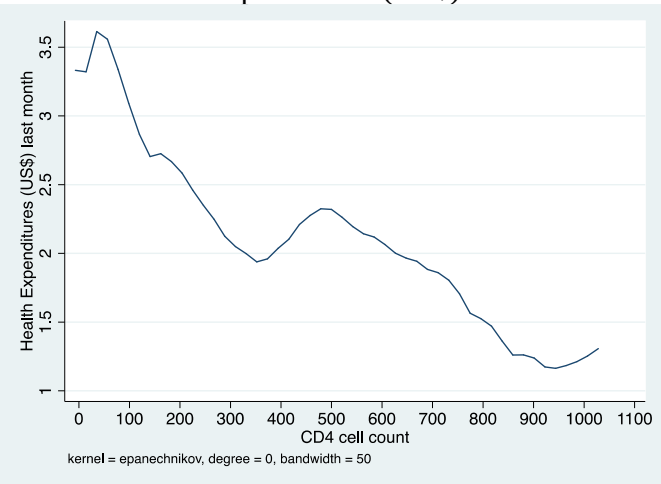

Panel B. Hours lost from usual activities due to illness last month




Panel C. Hours spent seeking/receiving care last month




Panel D. Health expenditures (US$) last month




**Note:** Outlying values for all variables were censored at 95$^{th}$ percentile

**Table 3.2. Employment of HIV-positive working-age adults compared to HIV-negative adults living in households with no infected household members**

| | Any work last week | | Any farm work last week | |
|---|---|---|---|---|
| | AOR | [95% CI] | AOR | [95% CI] |
| *HIV-, no HIV+ household member* | *Ref.* | | *Ref.* | |
| HIV+, CD4 ≤ 350 | 0.66*** | [0.54 - 0.80] | 0.64*** | [0.54 - 0.76] |
| HIV+, CD4 351-500 | 0.77** | [0.63 - 0.94] | 0.84* | [0.70 - 1.00] |
| HIV+, CD4 >500 | 1.10 | [0.93 - 1.29] | 0.90 | [0.78 - 1.04] |
| *Not on ART* | *Ref.* | | *Ref.* | |
| On ART | 1.23* | [1.03 - 1.45] | 1.25** | [1.08 - 1.45] |
| No. observations | 9,182 | | 9,182 | |
| *P-values from post-estimation Wald tests* | | | | |
| HIV+, CD4 ≤350 = HIV+, CD4 >500 | <0.001 | | <0.001 | |
| HIV+, CD4 351-500 = HIV+, CD4 >500 | <0.001 | | 0.402 | |

**Abbreviations:** AOR, adjusted odds ratio; 95% CI, 95% confidence interval, HIV+, HIV-positive; HIV-, HIV-negative; ART, antiretroviral therapy.

**Notes:** GEE regression models for working age adults (18-65 years old), with binomial distribution, logistic link, and exchangeable correlation at the household level. Reference group were HIV- participants who did not reside with HIV+ household members. Models controlled for education level, age, age-squared, gender, marital status, wealth index, number of children in household, number of household members and community indicators. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 3.3. Employment of HIV-negative working-age adults who have HIV-positive household members compared to HIV-negative adults living in households with no infected household members**

| | Any work last week | Any farm work last week |
|---|---|---|
| | AOR [95% CI] | AOR [95% CI] |
| *HIV-, no HIV+ household member* | *Ref.* | *Ref.* |
| HIV-, lives with HIV+ CD4 ≤350 | 0.71** [0.56 - 0.90] | 0.80* [0.64 - 1.00] |
| HIV-, lives with HIV+ CD4 351-500 | 0.68** [0.54 - 0.86] | 0.72** [0.58 - 0.90] |
| HIV-, lives with HIV+ CD4 >500 | 0.91 [0.75 - 1.10] | 0.96 [0.81 - 1.15] |
| *No household member on ART* | *Ref.* | *Ref.* |
| Some HIV+ household members on ART | 1.16 [0.70 - 1.91] | 1.09 [0.66 - 1.78] |
| All HIV+ household members on ART | 1.01 [0.81 - 1.25] | 0.99 [0.81 - 1.22] |
| No. observations | 7,874 | 7,874 |
| *P-values from post-estimation Wald tests* | | |
| HIV-, CD4 ≤350 = HIV-, CD4 >500 | 0.050 | 0.113 |
| HIV-, CD4 351-500 = HIV-, CD4 >500 | 0.023 | 0.016 |

**Abbreviations**: AOR, adjusted odds ratio; 95% CI, 95% confidence interval, HIV+, HIV-positive; HIV-, HIV-negative; ART, antiretroviral therapy.

**Notes:** GEE regression models for working age adults (18-65 years old), with binomial distribution, logistic link, and exchangeable correlation at the household level. Reference group were HIV- participants who did not reside with HIV+ household members. Models controlled for education level, age, age-squared, gender, marital status, wealth index, number of children in household, number of household members, and community indicators. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 3.4. Illness and health seeking behaviors of HIV-positive working-age adults compared to HIV-negative adults living in households with no infected household members**

| | Experienced illness last month | Lost time from usual activities due to illness last month [a] | Sought or received care last month | Spent money on healthcare last month | Hospitalized last year [c] |
|---|---|---|---|---|---|
| | AOR [95%CI] | AOR [95%CI] | AOR [95%CI] | AOR [95%CI] | AOR [95%CI] |
| *HIV-, no HIV+ household member* | *Ref.* | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| HIV+, CD4 ≤350 | 1.60*** [1.35 - 1.90] | 1.58*** [1.31 - 1.90] | 1.78*** [1.48 - 2.13] | 1.62***[1.34 - 1.95] | 2.32*** [1.79 - 3.02] |
| HIV+, CD4 351-500 | 1.52*** [1.28 - 1.81] | 1.47*** [1.22 - 1.78] | 1.67*** [1.38 - 2.01] | 1.67***[1.39 - 2.02] | 1.74*** [1.32 - 2.30] |
| HIV+, CD4 >500 | 1.18* [1.02 - 1.35] | 1.24** [1.06 - 1.44] | 1.31*** [1.12 - 1.53] | 1.27** [1.08 - 1.48] | 1.37** [1.09 - 1.73] |
| *Not on ART* | *Ref.* | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| On ART | 1.09 [0.94 - 1.26] | 1.11 [0.94 - 1.30] | 1.20* [1.03 - 1.41] | 1.14 [0.97 - 1.33] | 1.19 [0.95 - 1.48] |
| No. observations | 9,182 | 9,182 | 9,182 | 9,182 | 9,182 |
| *P-values for post-estimation Wald tests* | | | | | |
| CD4 ≤350 = CD4 >500 | <0.001 | 0.010 | <0.001 | 0.009 | <0.001 |
| CD4 351-500=CD4 >500 | 0.003 | 0.068 | 0.010 | 0.003 | 0.083 |

**Abbreviations:** AOR, adjusted odds ratio; CI, confidence interval; HIV+, HIV-positive; HIV-, HIV-negative; ART, antiretroviral therapy

**Notes:** GEE regression models for working age adults (18-65 years old), with binomial distribution, logistic link, and exchangeable correlation at the household level. Reference group were HIV- participants who did not reside with HIV+ household members. Models controlled for education, age, age-squared, gender, marital status, wealth index, number of children in household, number of household members, and community indicators. Usual activities include paid and unpaid work. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 3.5. Illness and health seeking behaviors of HIV-negative working-age adults who have HIV-positive household members compared to HIV-negative adults living in households with no infected household members**

| | Experienced illness last month | Lost time from usual activities due to illness last month [a] | Sought or received care last month | Spent money on healthcare last month | Hospitalized last year [c] |
|---|---|---|---|---|---|
| | AOR [95%CI] | AOR [95%CI] | AOR [95%CI] | AOR [95%CI] | AOR [95%CI] |
| *HIV-, no HIV+ household member* | *Ref.* | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| HIV-, lives with HIV+ CD4 ≤350 | 0.75* [0.58 - 0.97] | 0.77 [0.57 - 1.04] | 0.94 [0.71 - 1.25] | 0.86 [0.64 - 1.15] | 0.89 [0.56 - 1.41] |
| HIV-, lives with HIV+ CD4 351-500 | 0.75* [0.58 - 0.96] | 0.68*[0.50 - 0.92] | 0.75 [0.55 - 1.02] | 0.72*[0.53 - 0.98] | 0.93 [0.58 - 1.48] |
| HIV-, lives with HIV+ CD4 >500 | 0.83 [0.68 - 1.01] | 0.87 [0.69 - 1.09] | 0.93 [0.74 - 1.17] | 0.91 [0.73 - 1.15] | 0.97 [0.68 - 1.39] |
| *No household member on ART* | *Ref.* | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| Some HIV+ household members on ART | 0.97 [0.53 - 1.78] | 0.92 [0.43 - 1.97] | 0.81 [0.38 - 1.75] | 0.78 [0.36 - 1.68] | 0.43 [0.10 - 1.85] |
| All HIV+ household members on ART | 1.27* [1.01 - 1.60] | 1.27 [0.97 - 1.67] | 1.15 [0.88 - 1.50] | 1.19 [0.91 - 1.56] | 0.94 [0.61 - 1.44] |
| No. observations | 7,878 | 7,878 | 7,878 | 7,878 | 7,878 |
| *P-values for post-estimation Wald tests* | | | | | |
| HIV-, CD4 ≤350 = HIV-, CD4 >-500 | 0.492 | 0.443 | 0.957 | 0.709 | 0.724 |
| HIV-, CD4 351-500 = HIV-, CD4>500 | 0.457 | 0.137 | 0.194 | 0.166 | 0.851 |

**Abbreviations:** AOR, adjusted odds ratio; CI, confidence interval; HIV+, HIV-positive; HIV-, HIV-negative; ART, antiretroviral therapy

**Notes:** GEE regression models for working age adults (18-65 years old), with binomial distribution, logistic link, and exchangeable correlation at the household level. Reference group were HIV- participants who did not reside with HIV+ household members. Models controlled for education, age, age-squared, gender, marital status, wealth index, number of children in household, number of household members, and community indicators. Usual activities include paid and unpaid work.

**Table 3.6. Economic outcomes of HIV-positive working-age adults, stratified by ART initiation status and viral load suppression status, compared to HIV-negative adults living in households with no infected household members**

**Panel A: ART STRATIFICATION**

| Study group | Any work last week | Lost time from usual activities due to illness last month [a] | Spent money on healthcare last month |
|---|---|---|---|
| | AOR [95% CI] | AOR [95% CI] | AOR [95% CI] |
| *HIV-, no HIV+ in HH* | *Ref.* | *Ref.* | *Ref.* |
| HIV+, CD4<=350, not on ART | 0.66*** [0.52 - 0.83] | 1.82*** [1.46 - 2.27] | 1.86*** [1.50 - 2.32] |
| HIV+, CD4<=350, on ART | 0.80 [0.63 - 1.02] | 1.51*** [1.20 - 1.90] | 1.59*** [1.27 - 2.00] |
| HIV+, CD4351-500, not on ART | 0.75* [0.59 - 0.95] | 1.46** [1.16 - 1.84] | 1.69*** [1.34 - 2.11] |
| HIV+, CD4351-500, on ART | 0.98 [0.76 - 1.26] | 1.65*** [1.31 - 2.09] | 1.89*** [1.50 - 2.38] |
| HIV+, CD4>500, not on ART | 1.11 [0.93 - 1.32] | 1.15 [0.97 - 1.37] | 1.17 [0.98 - 1.39] |
| HIV+, CD4>500, on ART | 1.32** [1.07 - 1.63] | 1.49*** [1.23 - 1.80] | 1.58*** [1.31 - 1.90] |
| Observations | 9,182 | 9,182 | 9,182 |
| *P-values for post-estimation Wald tests* | | | |
| CD4 351-500, not on ART = CD4 >500, not on ART | 0.004 | 0.081 | 0.006 |
| CD4 >500, not on ART = CD4 >500, on ART | 0.170 | 0.028 | 0.009 |

**Panel B: VIRAL LOAD STRATIFICATION**

| Study group | Any work last week | Lost time from usual activities due to illness last month [a] | Spent money on healthcare last month |
|---|---|---|---|
| | AOR [95% CI] | AOR [95% CI] | AOR [95% CI] |
| *HIV-, no HIV+ in HH* | *Ref.* | *Ref.* | *Ref.* |
| HIV+, CD4 <=350, DVL | 0.71** [0.57 - 0.90] | 2.01*** [1.63 - 2.49] | 2.05*** [1.66 - 2.54] |
| HIV+, CD4 <=350, UVL | 0.67** [0.50 - 0.88] | 1.33* [1.01 - 1.75] | 1.31 [1.00 - 1.73] |
| HIV+, CD4 351-500, DVL | 0.81 [0.63 - 1.05] | 1.48** [1.15 - 1.89] | 1.65*** [1.29 - 2.10] |
| HIV+, CD4 351-500, UVL | 0.88 [0.68 - 1.15] | 1.69*** [1.32 - 2.15] | 1.88*** [1.47 - 2.39] |
| HIV+, CD4>500, DVL | 1.21 [0.99 - 1.47] | 1.22 [1.00 - 1.48] | 1.16 [0.95 - 1.41] |
| HIV+, CD4>500, UVL | 1.14 [0.94 - 1.40] | 1.37*** [1.14 - 1.65] | 1.45*** [1.21 - 1.74] |
| Observations | 8,708 | 8,708 | 8,708 |
| *P-values for post-estimation Wald tests* | | | |
| CD4 351-500, DVL = CD4 >500, DVL | 0.010 | 0.195 | 0.017 |
| CD4 >500, DVL = CD4>500, UVL | 0.678 | 0.334 | 0.069 |

**Abbreviations:** AOR, adjusted odds ratio; CI, confidence interval; HIV+, HIV-positive; HIV-, HIV-negative; ART, antiretroviral therapy **Notes:** GEE regression models for working age adults (18-65 years old), with binomial distribution, logistic link, and exchangeable correlation at the household level. Reference group are HIV- participants who do not reside with HIV+ household members. Models controlled for education, age, age-squared, gender, marital status, wealth index, number of children in household, number of household members, and community indicators. Usual activities include paid and unpaid work.

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# CHAPTER 4: IMPACT OF TEST-AND-TREAT INTERVENTION ON INVESTMENTS IN HUMAN CAPITAL: EVIDENCE FROM THE SEARCH TRIAL

## 4.1 Overview

**Background:** Improved health and life expectancies that result from expanded HIV testing and treatment (the test-and-treat strategy) could be important determinants of human capital investments in low-income countries. Furthermore, better economic functioning of populations that have wider access to HIV testing and treatment could offer the means for families in low-income countries to invest more in their children's education. We used data from a cluster randomized trial of the HIV test-and-treat strategy in rural Uganda and Kenya (NCT01864603) to investigate whether the test-and-treat strategy improved investments in child education.

**Methods:** We used longitudinal data from the Sustainable East Africa Research in Community Health Study (SEARCH) trial where half communities were randomized to receive the annual HIV testing, treatment upon diagnosis, and streamlined delivery of healthcare while other half of communities received standard of care. We evaluated school attendance, primary school completion, secondary school completion, and school expenditures among a cohort of HIV-negative children who were 9-16 years old at baseline. Children were categorized into study groups based on HIV status and viral load suppression status of the adults in their households. We focused on households with HIV-positive adults who had detectable viral load at baseline (i.e., were in need of ART) and we also examined children whose biological parent had HIV and detectable viral load. We used a difference-in-differences design to compare trends in the intervention communities to trends in control communities over a four-year period. Linear

regression models with individual fixed effects also controlled for all time-invariant child characteristics that may have affected their schooling outcomes.

**Results:** We used data from 4,554 children residing in 2,571 households, for a total of 15,003 person-year observations from 15 intervention and 15 control communities. Overall, we found positive impacts of the test-and-treat intervention on education outcomes. Children in the intervention communities had a higher probability of completing primary school and having at least some secondary school education. For example, children who lived in households with an adult who had detectable viral load had 6 percentage points increase in probability of finishing primary school in the intervention communities at one year follow-up (FUY1) ($p$-val <0.05), 9 percentage points increase at FUY2 ($p$-val <0.01), and 11 percentage points increase ($p$-val <0.01) at FUY3. In the last year of follow-up, the probability of having at least some secondary school education was 13 percentage points higher for children whose mother had detectable viral load ($p$-val <0.01) and 14 percentage points higher when their father had detectable viral load ($p$-val <0.01). Although both boys and girls in households with an HIV-positive adult benefitted from the intervention, boys in the intervention communities had statistically significant higher gains in terms of finishing primary school and at least some secondary school than girls.

The average annual school expenditures per child in the intervention communities increased by $7 USD at FUY1, ($p$-val <0.01), $6 USD at FUY2 ($p$-val <0.05), and $9 USD at FUY3 ($p$-val <0.01). The effect of the intervention was larger for children who lived with an HIV-positive adult and even larger for children who lived with an adult with detectable viral load at baseline. School expenditures for children of biological mothers who had HIV and detectable viral load increased by $19 USD at FUY1 ($p$-val <0.001), $18 USD at FUY2 ($p$-val =0.076), and $36 USD at FUY3 ($p$-val <0.05).

**Conclusions:** This study documents a large and meaningful impact of the test-and-treat intervention on investments in human capital. Children in the intervention communities had a higher probability of completing primary school and higher probability of having at least some secondary education. Furthermore, average school expenditures were higher in the intervention communities. The results indicate that investments in test-and-treat could have multigenerational spillover effects with implications for economic development in low-income countries.

## 4.2 Background

Evidence about the important prevention and health benefits of early antiretroviral treatment (ART) [1-3] was the foundation for 2015 WHO guidelines that recommend treatment for all persons living with HIV, and the UNAIDS 90-90-90 targets to rapidly scale-up HIV testing and treatment [4, 5]. Yet progress towards adopting the new guidelines has been slow in sub-Saharan Africa (SSA) [6], as many countries remain concerned about the required investment [4, 7-9]. Although the test-and-treat strategy offers a way to potentially shift the HIV epidemic, it also comes with a high financial cost of providing life-long medications to broader sections of the population and a high burden on health systems. Potential cuts to funding levels of the President's Emergency Plan For AIDS Relief (PEPFAR) and other US-based initiatives [10] could further undermine progress towards expanding access to testing and treatment. Understanding how early access to ART affects household economic functioning, including investments in human capital, will provide much needed evidence about the possible returns on investments in this strategy.

Improved health and life expectancy that result from early access to ART could be important determinants of human capital investments [11, 12]. Beyond that, early ART initiation could result in an economic boost to households and communities affected by HIV. Evidence from SSA indicates that ART initiation among people with low CD4 counts, in line with

historical WHO guidelines, leads to dramatically improved individual- and household-level economic outcomes [13-20] in terms of labor force participation, income, and quality of life for the individuals receiving ART. A limited number of studies have also documented benefits to household members of treated adults, particularly in the form of reduced domestic labor burden [21] and increased school enrollment for children [22]. Furthermore, some evidence indicates that ART expansion led to increased work hours of HIV-negative people whose households did not directly benefit from the treatment [23] and that ART availability significantly increased savings and investments in child schooling among HIV-negative individuals [24]. Maintaining good health status through early access to ART may amplify these economic benefits and provide the means to individuals in low-income settings to invest more in children's education.

We used longitudinal data from the Sustainable East Africa Research in Community Health Study (SEARCH) trial, a cluster randomized trial of the test-and-treat strategy in rural Uganda and Kenya, to evaluate the impact of the intervention on child school enrollment, primary school completion, at least some secondary school completed, and annual school expenditures. The intervention integrated population-wide community health campaigns that included HIV tests, ART initiation offered to all HIV-positive people upon diagnosis, and streamlined care approach that reduced many barriers to linking and retaining patients in treatment. Preliminary analyses from the SEARCH trial indicated that households in the intervention communities had high levels of retention in care [25], increased viral suppression [26], lower economic burden of care-seeking [27], and improved expectations about future health and longevity [28]. Baseline data also showed that high CD4 count was associated with substantial economic benefits for HIV-positive adults and their HIV-negative adult household (Chapter 3). The longitudinal SEARCH data enabled us to test whether the health and economic

benefits of test-and-treat had spillover effects to household decisions regarding investments in human capital.

### 4.3 Methods

#### 4.3.1 Study procedures

Data were collected from households in 32 rural communities participating in the ongoing SEARCH HIV test-and-treat cluster randomized controlled trial (NCT01864603). SEARCH data were collected at 12-month intervals for a total of 4 study waves in 16 intervention and 16 control communities from three non-adjacent geographic regions in Uganda and Kenya. The trial procedures are described in detail elsewhere [29]. Briefly, study communities consisting of approximately 10,000 individuals each were located in three distinct geographic regions with varying HIV prevalence; 12 communities were in western Kenya, 10 in eastern Uganda, and 10 in southwestern Uganda. At the beginning of the trial (baseline), all communities received census and population-wide HIV testing. The "hybrid" testing approach, which involved multi-disease community health campaigns (CHCs) and home-based testing of participants who did not attend CHC, resulted in 89% of the population living in the study communities having tested at baseline [29].

In the intervention communities, HIV positive individuals were referred to care immediately upon diagnosis and were then offered immediate ART initiation or continuation of ART at the clinic using a streamlined care approach. The Streamlined ART model was designed to reduce barriers to care, including reduced wait time, quarterly (as opposed to monthly) follow-up visits, patient-centered approach to care, phone hotline, appointment reminders by phone/SMS, provision of viral load results, and follow-up to missed appointments. The CHCs were repeated every year in the intervention communities and newly identified HIV patients were enrolled in Streamlined ART. The control communities followed country guidelines for

testing and referral to care, ART initiation at CD4 counts <500 cells, and standard procedures for delivering treatment to HIV patients.

Following the CHCs and in parallel with home-based testing, a random sample of households with and without an HIV-positive adult were selected for structured household surveys that were administered to adults in the household. In each SEARCH community, we conducted surveys with 100 households that included an HIV-positive adult and 100 households that did not include an HIV-positive adult. The household surveys sought to assess socio-economic conditions of households and individuals residing in them. They consisted of several sections that obtained information on individuals' demographic characteristics, employment and income of household members aged ≥12 years, ownership of durable goods and livestock, health care utilization, and education of household members aged 6-25 years. Reports were obtained for all household members from one person, typically the household head or spouse of household head. These surveys were adapted from The World Bank's Living Standards Measurement Surveys that have been administered to households in many low- and middle-income countries [30]. Survey questionnaires were administered by trained research assistants who visited homes of selected participants. Information collected in household surveys was linked at the individual level to SEARCH data on HIV status, and for HIV-positive individuals, on CD4 count.

### 4.3.2 Ethics statement

The Makerere University School of Medicine Research and Ethics Committee (Uganda), the Ugandan National Council for Science and Technology (Uganda), the Kenya Medical Research Institute Scientific Ethics Review Unit (Kenya), and the University of California San Francisco Committee on Human Research (USA) approved the consent procedures and the study. All participants provided verbal informed consent in their preferred language with a signature or fingerprint confirmation of consent.

### 4.3.3 Study groups

We used baseline age of children as well as HIV status and viral load of children and adults residing in the same households to define our study groups. We began by defining a cohort of HIV-negative children aged 9-16 years at baseline and focused on education outcomes of these children over the four-year study period. In Uganda, primary education is designed to take place during ages 6-12 years and in Kenya during 6-13 years, but in practice many children begin school later and grade repetition is quite common. According to World Bank data, 26% of students in Kenya and 14% of students in Uganda are older than the official school age range, and 5% of students in Kenya and 7% of students in Uganda are repeating grades [31] This what? means that many pupils in classes are older than the intended age, sometimes by many years, which puts them at an even greater risk of dropping out before completion of primary education [32]. Following the cohort of children 9-16 years old at baseline enabled us to measure outcomes of children who could plausibly complete primary school and enroll in secondary school during the follow-up period. The World Bank data indicate that while most children who complete primary education in Kenya progress to secondary education, only half of children in Uganda do so [31]. Furthermore, while most children who start school in Kenya persist to the last grade of primary school, only 21% of children in Uganda do so [31]. Thus, we hypothesized that children in the 9-16 years at baseline cohort were especially at risk of dropping out of school and that the intervention had the potential to impact education outcomes of children in this age group.

Analyses were limited to HIV-negative participants because we wanted to explore intergenerational investments in human capital as a function of adult health and treatment status. HIV-positive children might instead be influenced by various different factors that affect education outcomes, such as own health and stigma. Finally, we eliminated from the sample

children who had suspected errors in their basic demographics over time (e.g. gender varied from wave to wave, age differed by +/- 5 years from wave to wave).

We used baseline HIV status of adults to categorize children into HIV-positive households (i.e. it had at least one HIV-positive adult household member at baseline). HIV status of individuals was determined by rapid HIV tests obtained using the hybrid testing approach, i.e. CHCs and home-based testing, described above. For simplicity of analysis and interpretation, we excluded X# households with ≥2 HIV-positive adults. We then used viral load of HIV-positive adults to identify adults whose viral load were not suppressed (i.e. above 500 copies/mL), which suggested that they were not receiving ART at baseline. HIV RNA levels were measured as previously described [33]. Finally, for a subset of children who resided with their biological parents, we used HIV-status and viral load to identify children who lived with HIV-infected mother or father who were in need of HIV treatment. This additional analysis was done to test whether HIV-infection of the primary caretaker affects investments in child education differently from HIV-infection of some other adult household resident.

**4.3.4 Outcome measures**

We assessed four different education outcomes for each child: school participation, primary school completion, having at least some secondary school education, and annual school expenditures. We measured school participation using a binary indicator of whether a child was attending school in a given study wave. Primary school completion was defined using a binary indicator. We defined a binary indicator for having at least some secondary education if children had completed any grade above primary school. School expenditures were captured using a continuous measure of the amount of annual school expenditures for each child reported by the survey respondent (conversions to US dollars were made using exchange rates from April of each study wave).

### 4.3.5 Statistical analysis

We began by examining the study outcomes over time in the intervention and control communities using nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing). We then tested the effect of the test-and-treat intervention on study outcomes over time by fitting linear regression models:

$$(1)\ Y_{ihjt} = \alpha_i + \mu_1 INTERVENTION_j * WAVE\ 1 + \mu_2 INTERVENTION_j * WAVE\ 2 + \mu_3 INTERVENTION_j * WAVE\ 3 + \varphi X_{hjt} + \gamma_t + \varepsilon_{hjt}$$

where $Y_{ihjt}$ was the outcome variable (school enrollment, completed primary school, and completed at least some secondary school, school expenditures). The $INTERVENTION_j$ variable was set to 1 if child *i* resided in a randomly selected household *h* in community *j* that was either randomized to HIV test-and-treat intervention or control communities. *WAVE 0* was an indicator for baseline wave, *WAVE 1* was an indicator for follow-up year 1 wave (FUY1), *WAVE 2* was an indicator for follow-up year 2 wave (FUY2), and *WAVE 3* was an indicator for follow-up year 3 wave (FUY3). $\alpha_i$ was the individual-level fixed effect controlling for all time-invariant child characteristics and $\gamma_t$ was a full set of study wave fixed effects to account for secular trends. Our models included indicators for the month of interview to control for seasonal trends, an indicator for school breaks, and the proportion of household members who were children to control for multiple children competing for household resources.

We determined the effect of the intervention separately in eight study groups of interest: (1) all households; (2) households where all adults were HIV-negative; (3) households with an HIV-positive adult; (4) households with an HIV-positive adult who had detectable viral load; (5) households where biological parent had HIV; (6) households where biological parent had

detectable viral load; (7) households where biological mother had detectable viral load, (8) households where biological father had detectable viral load. We then repeated the regression models separately for boys and girls. We performed sensitivity analyses using a broader sample of children 9-20 years old and a sample that included individuals with suspected data errors.

## 4.4 Results

### 4.4.1 Study participants

Data were collected between July 2013 and June 2017 for 8,019 children aged 9-16 years old at baseline, who lived in 3,902 households, totaling n=27,255 child-wave observations over the full study period. Our sample represented approximately 10% of the full SEARCH trial population. We omitted from the analysis households with HIV-positive children (n=25,714 child-wave observations) and households with multiple HIV-positive adults (n=22,955 observations), and children with unknown HIV status (n=16,822 observations). We dropped from the analysis two communities (one intervention and one control) in Kenya where the final wave of data were not collected due to logistical problems (n=16,151 observations) and individuals with possible data errors (n= 15,003 observations). Our final analytic cohort of children 9-16 years old at baseline included 15,003 child-wave observations, from 4,554 unique children, residing in 2,571 households.

### 4.4.2 Descriptive statistics

The average age of children in the study cohort was 12 years at baseline and 15 years at FUY3 (Table 4.1). Approximately 40 percent of children lived in a household with an HIV-positive adult and 27% lived in a household with HIV-positive biological parent, reflecting the study sampling design. Approximately 10% of children in control communities and 12% of children in intervention communities lived in a household with an HIV-positive adult who had

detectable viral load at baseline. In households with HIV-positive adults, biological mothers were more likely to be infected than fathers (approximately 18% versus 9% at baseline).

At each study wave, the vast majority of children from both intervention and control communities reported attending some school during the previous year. At baseline, 7% of children in the control communities and 8% of children in intervention communities reported having completed primary school. By FUY3 these figures increased to 23% in control communities and 29% in intervention communities. Slightly fewer children reported having at least some secondary school completed, 6% at baseline and 22% at FUY3 in control communities and 7% at baseline and 28% at FUY3 in the intervention communities. Very few participants in the cohort (<1%) completed secondary school during the study period. Annual school expenditures per child increased over time, from $40 USD at baseline to $73 USD at FUY3 in control communities and $38 USD to $82 USD at FUY3 in intervention communities.

### 4.4.3 Regression results

Figure 4.1 presents trends in primary school completion and at least some secondary school completion at different ages, split by intervention and control communities at baseline and at FUY3. In general, the children in the intervention communities attained slightly higher education by FUY3. Differences in school completion at FUY3 became more apparent when we considered children who resided with an HIV-positive adult. In these households, children in the intervention communities completed primary and at least some secondary school at higher proportions than their counterparts in control communities. Higher completion rates of primary and at least some secondary school by children in intervention communities were clearly evident when we considered children who resided with an adult who had detectable viral loads, especially if that adult was the biological mother.

Figure 4.2 displays the proportion of boys and girls who completed primary school during the study period. The proportion of children who finished primary school increased overall from wave to wave as the cohort aged, but the increases were higher in the intervention communities compared to control communities, especially for boys whose fathers had detectable viral loads. The proportion of girls completing primary school was also increasing in general over time, but the differences between intervention and control communities were not as pronounced, except when the girls' mothers had detectable viral loads.

Figure 4.3 displays proportion of boys and girls who had at least some secondary education over time. In general, approximately equal proportion of boys in the intervention and control communities had some secondary education at baseline, but their trends diverged considerably over time, with boys in the intervention communities completing at least some secondary school at much higher rates. There appeared to be a heterogeneous effect of the intervention by gender over time, with completion of at least some secondary school having increased at higher rates for boys whose HIV-positive fathers had detectable viral load than for girls in these households. In households where mothers had detectable viral loads, girls appeared to have benefitted more from the intervention over time in terms of secondary school enrollment than boys. The effect of the intervention appeared to have been the strongest for sons of HIV-positive fathers with detectable viral load. More than 30% of boys in these households reached secondary school at FUY3 in the intervention communities compared to fewer than 8% in the control communities.

Figure 4.4 displays trends in annual school expenditures for boys and girls in intervention and control communities. Average annual spending on each child's education was increasing overall in all communities over time, but the increases were greater in the intervention

communities. The largest gains for both boys and girls appeared to have occurred in households where the biological mother had detectable viral load.

School participation trends appeared to be very similar in the intervention and control communities over time (Figure A in Appendix 2). Regression models with individual fixed effects also showed no differences in school participation trends. We found no differences in school participation between children in the intervention and control communities over the three years of follow-up (Table 4.2).

The SEARCH intervention had a significant impact on primary school completion of children in households with HIV-positive adults (Table 4.3). In households where an HIV-positive adult with detectable viral load resided, the probability of primary school completion in the intervention communities increased by 5 percentage points ($p$-val <0.05) at FUY1, 7 percentage points ($p$-val <0.01) at FUY2, and 10 percentage points ($p$-val <0.001) at FUY3. The magnitude of the intervention effect was higher for children in households where an HIV-positive biological parent had detectable viral load, especially if that parent was the mother.

The intervention also led to an increase in the probability of completing some secondary school (Table 4.4), with children in HIV-positive households in the intervention communities having 6 percentage points ($p$-val <0.01) higher probability of completing at least some secondary education at FUY3 compared to their counterparts in control communities. In households where the HIV-positive adult had detectable viral load, probability of having at least some secondary education increased by 6 percentage points ($p$-val <0.05) at FUY1, 8 percentage points ($p$-val <0.001) at FUY2, and 11 percentage points ($p$-val <0.001) at FUY3. The impact of the intervention on completing any secondary school was especially evident in households where

the biological mothers or fathers had detectable viral load (13 percentage points increase at FUY3, p-val <0.01, and 14 percentage points increase at FUY3, p-val <0.05, respectively).

Annual school expenditures increased at higher rates in the intervention communities than in the control communities (Table 4.3). Households in the intervention communities spent on average $7 USD more (*p*-val <0.01) per child's education at FUY1, $6 USD more (*p*-val <0.05) at FUY2, and $9 USD more (*p*-val <0.01) at FUY3. The impact of the intervention was much stronger for children in HIV-positive households where adults had detectable viral load, especially when that adult was the biological parent. When the biological mother had detectable viral load at baseline, investments in children's education increased on average in the intervention communities by $19 USD per child (*p*-val <0.001) at FUY1, $18 USD (*p*-val =0.076) at FUY2, and $36 USD (*p*-val <0.05) at FUY1.

Impact of the intervention was much stronger for boys than girls in terms of primary school completion and any secondary school completion (Tables 4.6 and 4.7). For example, among girls in households where either parent had detectable viral load, the probability of primary school completion increased by 5 percentage points at FUY2 and 7 percentage points at FUY3, but these differences were not statistically significant. In contrast, boys' probability of completing primary education increased by 11 percentage points (*p*-val <0.01) at FUY1, 13 percentage points (*p*-val <0.01) at FUY2, 15 percentage points (*p*-val <0.01) at FUY3. Girls in the intervention communities had 14 percentage points higher (*p*-val <0.05) chances of completing any secondary school at FUY3 if their mothers had detectable viral load at baseline. It is noteworthy that our power was very limited in the stratified models, which might explain why some of the differences were not statistically significant.

Boys in the intervention communities were generally completing school at much higher rates than boys in the control communities, but the differences were especially sticking in households where fathers had detectable viral load. Primary school completion increased by 20 percentage points ($p$-val <0.01) at FUY3 and completion of any secondary school increased by 21 percentage points ($p$-val <0.01) at FUY3 for boys in the intervention communities whose fathers had detectable viral loads compared their counterparts in control communities.

In models of school expenditures that were stratified by gender, we found that annual expenditures on education were much higher for both boys and girls in the intervention communities than in the control communities (Table 4.8). For example, households where a parent had detectable viral load at baseline invested $31 more ($p$-val <0.05) in their daughters' education at FUY3 and $24 more ($p$-val <0.05) in their sons' education at FUY3. In models stratified by study country, we found that the effect of the intervention on school completion was generally stronger in Uganda than in Kenya. On the other hand, school expenditures in the intervention communities increased relatively more in Kenya than in Uganda. Results did not change when we included children with possible data entry errors in the sample. These participants were omitted from the main analysis due to concerns about measurement errors, which are particularly problematic in panel data.

**4.5 Discussion**

Our study findings indicated that the test-and-treat intervention had a large and meaningful impact on parents' investments in children's education, an important form of human capital. We found that children who resided with an HIV-infected adult in intervention communities had significantly improved schooling outcomes than their counterparts in control communities. Participants who benefitted the most in intervention communities were children whose biological parents were HIV-positive and in need of ART at baseline (i.e. had detectable

viral load at baseline). We also found that the intervention led to significantly higher expenditures on children's education, especially when the biological mother was in need of ART. These findings suggest that the direct health and prevention benefits of test-and-treat have spillover effects that extend well beyond the individual adult receiving treatment; these effects could have multi-generational impacts on children's education outcomes and lifetime earnings. Our findings provide further justification for investment in HIV test-and-treat interventions, strengthening health systems to satisfy the increased demand for healthcare, and improving the quality of care to ensure retention and adherence to ART.

The HIV epidemic has had a devastating impact on morbidity and mortality in sub-Saharan Africa, leaving millions of children orphaned and shifting the average life expectancy on the continent [34]. Previous studies have documented that parental illness and death led to decreased school participation, especially if the deceased parent was the mother [35, 36]. The crucial role mothers play in their children's education was also evident in our study findings. The intervention had the greatest impact on primary school completion when we considered households where the biological mother had detectable viral load status. In relative terms, the probability of completing primary school among children whose mothers needed ART at baseline increased from baseline mean of 7.2% by a factor of 1.4 times at FUY1 (or 9.8 percentage point increase), 1.6 times at FUY2 (or 11.9 percentage point increase), and 1.8 times at FUY3 (or 13.4 percentage point increase) in the intervention communities compared to control communities. The probability of completing at least some secondary school more than doubled at FUY3 for children in the intervention communities whose mothers or fathers needed ART at baseline, compared to their counterparts in the control communities.

The differences between children in intervention and control communities were the most evident when we compared school expenditures in households where HIV-positive mothers needed ART at baseline. By the final year of follow-up, children of HIV-positive mothers with detectable viral load received $36 USD more for education than children in the control communities, even after adjusting for the overall increases in school expenditures over time in both study arms. At baseline, the average school expenditures in the intervention communities equaled $38 USD. This means that the additional $36 increase in the intervention communities represented nearly a doubling (93% increase relative to baseline mean) in school investments just three years after implementation of test-and-treat. The large increases in school expenditures could be explained in some part by more children in the intervention communities enrolling in secondary school, which typically costs considerably more than primary school. Another reason for the increased expenditures could have been that mothers sent their children to better quality schools, which would have likely resulted in even better education of children in the intervention communities.

Some of our most striking findings were from models stratified by gender, especially for boys whose fathers had detectable viral load at baseline. The probability of completing primary school increased for these boys in the intervention communities by a factor of 3 at FUY2 and FUY3 compared to their counterparts in control communities. Furthermore, their probability of completing at least some secondary school increased in the intervention communities by a factor of 2.6 at FUY1, by a factor of 5.1 at FUY2, and by a factor of 5.8 at FUY3 compared to control communities. The graphs representing school completion trends over time clearly display the tremendous gains made by these boys in the intervention communities. For example, in Figure 4.3, the probability of completing any secondary school was increasing steeply over time in the

intervention communities for boys whose fathers needed ART at baseline, but the time trend was flat, at about 4%, throughout the study period for their counterparts in the control communities. Among girls whose mothers had detectable viral loads, probability of completing primary school increased by a factor of 3.6 and probability of completing at least some secondary school increased by a factor of 4.2 compared to their counterparts in control communities.

Interim SEARCH analyses of the primary study outcomes, which were limited to evaluating trends in the intervention communities, suggest that the test-and-treat strategy was associated with increased viral suppression, increased HIV diagnosis, improved linkage to ART initiation [26], high levels of retention in care [25], and lower economic burden of care-seeking [27]. Furthermore, an economic evaluation of subjective life-expectations found that people in the test-and-treat intervention communities had improved expectations about future health and longevity at FUY1 [28]. The findings from this study are consistent with the hypothesis that the health and economic outcomes of households, and possibly adults' subjective expectations about the future, are important determinants of investments in children's schooling [11, 37]. Also consistent with existing literature is the finding that HIV has a higher effect on human capital investments in boys [34]. Previous studies indicate that higher risk of mortality negatively impacts school outcomes [34]. We found that investments in human capital significantly increased after four years of communities receiving the HIV test-and-treat intervention. A possible explanation of this finding is that longer time horizons associated with the health and prevention benefits of test-and-treat may have translated to improved perceptions about the returns of investments in education [34, 38, 39].

Another important mechanism though which the intervention may have increased investments in human capital could be higher productivity of adults in the households. That is, in

households where more adults continue to participate in labor force and fewer adults require care, more resources are available for education and fewer children are asked to leave school, either to substitute for adult labor or to care for ailing household members [21, 40-45]. Baseline data from the SEARCH trial showed that newly identified HIV-positive participants had comparable economic outcomes to HIV-negative participants. In contrast, HIV-positive participants whose health status had declined as they awaited treatment fared worse in terms of labor participation and resources spent to treat their symptoms (i.e. opportunity time, lost wages, and health expenditures). Furthermore, HIV-negative household members of people whose health status declined due to HIV also had worse economic outcomes. This evidence suggests that maintaining high CD4 counts may have had substantial economic benefits for HIV-positive adults and their HIV-negative adult household members. Improved economic functioning of households receiving the test-and-treat intervention may have provided families in the intervention communities the means to invest more in education. In households that struggle with ailing family members, children are often taken out of school to supplement lost labor [21, 40-45]. Our study provides evidence that avoiding the income shock that occurs when adults' health status declines as they await HIV treatment may have had a protective effect on children's education outcomes.

Our study had several limitations. First, we collected self-reported survey data which could have suffered from recall bias. We attempted to limit these biases by using short recall periods that are common in similar literature [46]. We also determined our study groups using laboratory-confirmed measures of HIV status and viral load to eliminate self-reported health status bias in these measures [37]. Second, we found that over time respondents made errors in reporting basic descriptive characteristics of some participants. In an effort to reduce noise of our

data, we omitted individuals who had such reporting errors from the analysis. However, in a sensitivity analysis we confirmed that our findings were robust to including the full sample of participants in our models. Third, we did not collect detailed data about exact grade the child was currently enrolled in (instead we asked broadly whether child was in lower primary, upper primary, etc.), which limited our ability to track kids' progress through the education system over time. Data on test scores and literacy were also not collected. At the same time, our data captured some key milestones of education, including completion of primary school, as well as entering and completing at least some secondary school. Future analyses should investigate whether test-and-treat strategy leads to improved cognition and literacy. Fourth, the vast majority of study participants reported still being in school at some point in the past year, which significantly reduced our ability to detect differences in current school enrollment rates between intervention and control communities. That is, the fact that nearly all children reported still being in school at some point during the previous year might explain why we did not detect an impact of the intervention on this study outcome.

Lastly, less than 1% of children in the study cohort completed secondary school, making evaluation of this outcome not feasible among the cohort of children 9-16 years old at baseline. We compared our data to the World Bank's indicators to ensure that our statistics were on par with other data sources. We found that our statistics were highly comparable among adults 25 years or older: secondary school completion in Kenya was 15% and in Uganda was 6% in our data compared to 18% and 6%, respectively, in the World Bank's data. Thus, we believe that the very low proportion of children in the study cohort who completed secondary school might have been due to the fact that we did not follow these children long enough to observe this outcome. When we considered secondary school completion among all school-aged participants (6-25

years old), we found that participants in the intervention communities had small but statistically significant increases in secondary school completion at FUY2 (0.9 percentage points, *p*-val <0.01) and at FUY3 (0.8 percentage points, *p*-val <0.05). This finding suggests that in the short run, test-and-treat might have had a small but positive impact on upper-level school completion. Future trials that have longer follow-up periods might enable analysis of the impact of test-and-treat on secondary school completion.

The results from this study provide causal evidence about the impact of the test-and-treat intervention on investments in human capital. We found that families in the intervention communities spent more on their children's education and that these investments translated to better school outcomes, including primary school completion and having at least some secondary school education. The largest impact of the intervention was among children whose biological parents needed treatment at baseline. Foster children who lived in the households, likely including many children who became orphans due to the HIV epidemic, might require additional investment in the form of cash transfers or other incentives and interventions. Previous studies have documented that orphans had especially poor school outcomes as HIV-related mortality increased [35, 47]. Our study suggests that early ART initiation of the biological parent may lead to significantly better education outcomes of their offspring.

In recent years, we have learned about the tremendous prevention and health benefits of early ART, both in controlled experiments and in population studies [1, 3]. Test-and-treat strategies for HIV offer a potential way to dramatically shift the HIV epidemic and ultimately eradicate the disease. With this evidence in hand, many countries are at a tipping point, where local governments and donors need to make a strong commitment to expand access to HIV testing and treatment, strengthen health systems to meet the increased demand of HIV patients,

and improve the quality of care to encourage patient retention and adherence. Donors, such as PEPFAR and the Global Fund, have played a key role in scaling-up access to ART and curbing the HIV epidemic in low-income countries; potential cuts to these programs at this crucial moment could prove to be catastrophic. In this study, we provided evidence that investing in test-and-treat has multigenerational impact on education. Improving health of adults who were infected with HIV and in need of treatment had a significant impact on decisions about the value of education in the same households. Children in the intervention communities who lived with a parent or another adult household member who had HIV had much better chances of completing primary school, completing at least some secondary school, and had higher school expenditures than children in similar households who lived in the control communities.

In just a few years, the children in our study cohort will become parents themselves. The fact that children in the intervention communities attained higher education bodes well for their earning potential, as well as their understanding of how disease spreads, and learning about prevention methods. Furthermore, healthier parents have healthier and better educated children [48]. Repeating this cycle could have tremendous implications for economic development of countries in Africa and bringing them out of poverty.

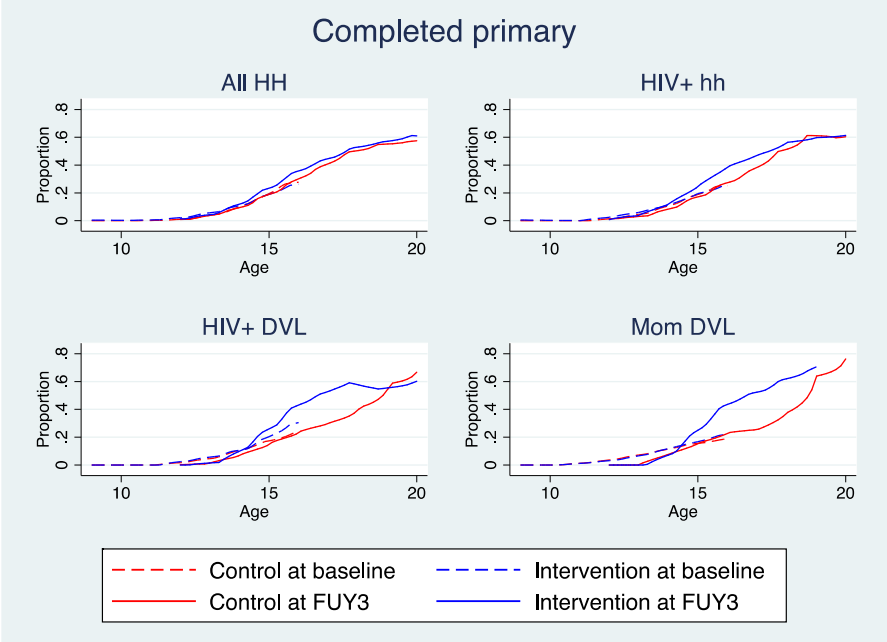
**Table 4.1. Descriptive characteristics of children 9-16 years old at baseline in control and intervention communities of the SEARCH trial over time**

| | Control communities (N=15) | | | | Intervention communities (N=15) | | | |
|---|---|---|---|---|---|---|---|---|
| | Baseline | FUY1 | FUY2 | FUY3 | Baseline | FUY1 | FUY2 | FUY3 |
| Individuals (N) | 2,347 | 1,971 | 1,820 | 1,609 | 2,207 | 1,874 | 1,704 | 1,471 |
| Households (N) | 1,308 | 1,140 | 1,102 | 990 | 1,263 | 1,102 | 1,034 | 933 |
| *Sample description* | | | | | | | | |
| Age, mean | 12.3 | 13.6 | 14.4 | 15.0 | 12.5 | 13.7 | 14.6 | 15.4 |
| Female, % | 49.2 | 47.9 | 47.6 | 45.6 | 49.1 | 48.6 | 48.3 | 46.2 |
| Proportion of household <18 years, % | 61.9 | 59.8 | 58.0 | 57.7 | 60.3 | 58.8 | 56.9 | 55.4 |
| HIV+ adult household, % | 40.1 | 39.1 | 38.7 | 39.0 | 42.0 | 41.9 | 41.5 | 39.7 |
| DVL adult household, % | 17.3 | 16.4 | 15.9 | 16.2 | 20.8 | 20.7 | 19.9 | 19.5 |
| HIV+ parent household, % | 26.4 | 26.4 | 26.3 | 26.6 | 26.4 | 27.7 | 27.9 | 27.6 |
| DVL parent household, % | 10.7 | 10.7 | 10.0 | 10.1 | 12.3 | 12.7 | 12.8 | 12.8 |
| HIV+ mother household, % | 17.5 | 17.5 | 17.4 | 18.0 | 18.2 | 19.1 | 19.7 | 18.5 |
| DVL mother household, % | 6.4 | 6.2 | 5.9 | 6.1 | 7.7 | 8.0 | 8.4 | 7.9 |
| HIV+ father household, % | 8.9 | 8.9 | 8.9 | 8.6 | 8.2 | 8.6 | 8.2 | 9.1 |
| DVL father household, % | 4.3 | 4.5 | 4.1 | 4.0 | 4.7 | 4.8 | 4.4 | 5.0 |
| *Unadjusted outcomes* | | | | | | | | |
| Attended school, % | 93.8 | 92.7 | 97.2 | 95.6 | 94.9 | 92.5 | 97.0 | 94.2 |
| Annual school expenditures, mean[a] | 39.8 | 46.1 | 57.1 | 73.9 | 37.7 | 51.3 | 59.9 | 82.9 |
| Completed primary, % | 6.7 | 12.5 | 18.6 | 23.1 | 7.7 | 14.7 | 23.0 | 28.7 |
| At least some secondary, % | 5.9 | 11.7 | 17.5 | 22.2 | 6.6 | 13.2 | 21.8 | 27.7 |
| Completed secondary, % | 0.0 | 0.2 | 0.3 | 0.7 | 0.1 | 0.1 | 0.6 | 0.6 |

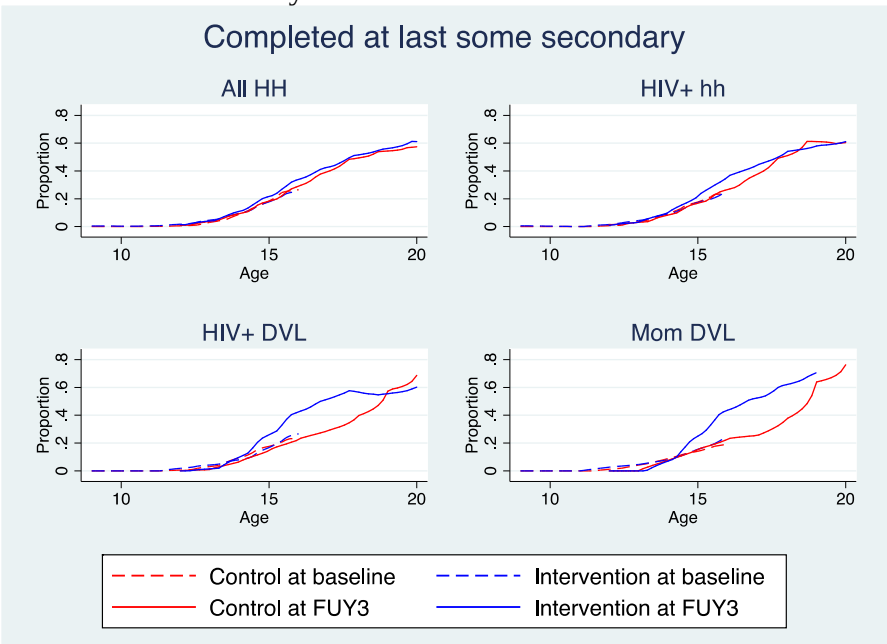
**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3.
**Notes:** SEARCH trial incorporated population-wide health campaigns, including HIV tests, at baseline in all communities. Intervention arm received repeated community-wide health campaigns at each study wave and streamlined care approach to linking HIV positive participants with treatment and ART delivery. Control communities received standard of care for HIV testing, linkage to care and ART delivery.
[a] Income and school expenditures are in USD.

**Figure 4.1. Proportion of children at different ages completing primary school (Panel A) and some secondary school (Panel B), at baseline and FUY3, in interventions vs. control communities.**

Panel A: Proportion of children at different ages who have completed primary school

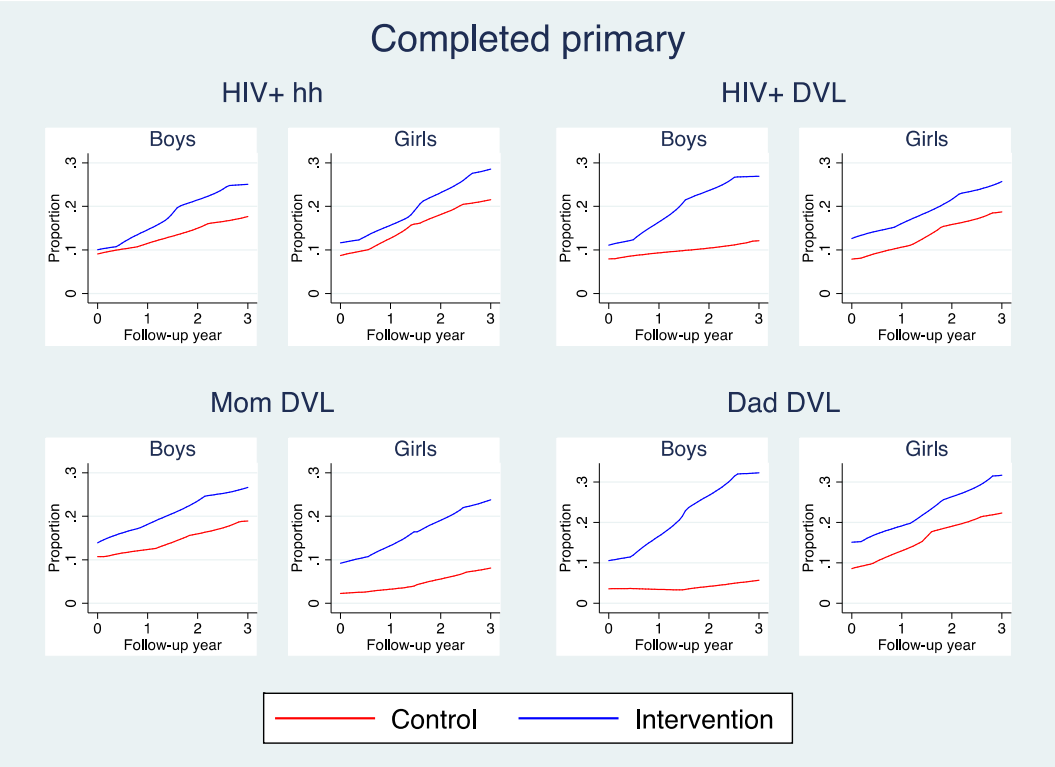



Panel B: Proportion of children at different ages who have completed at least some secondary school



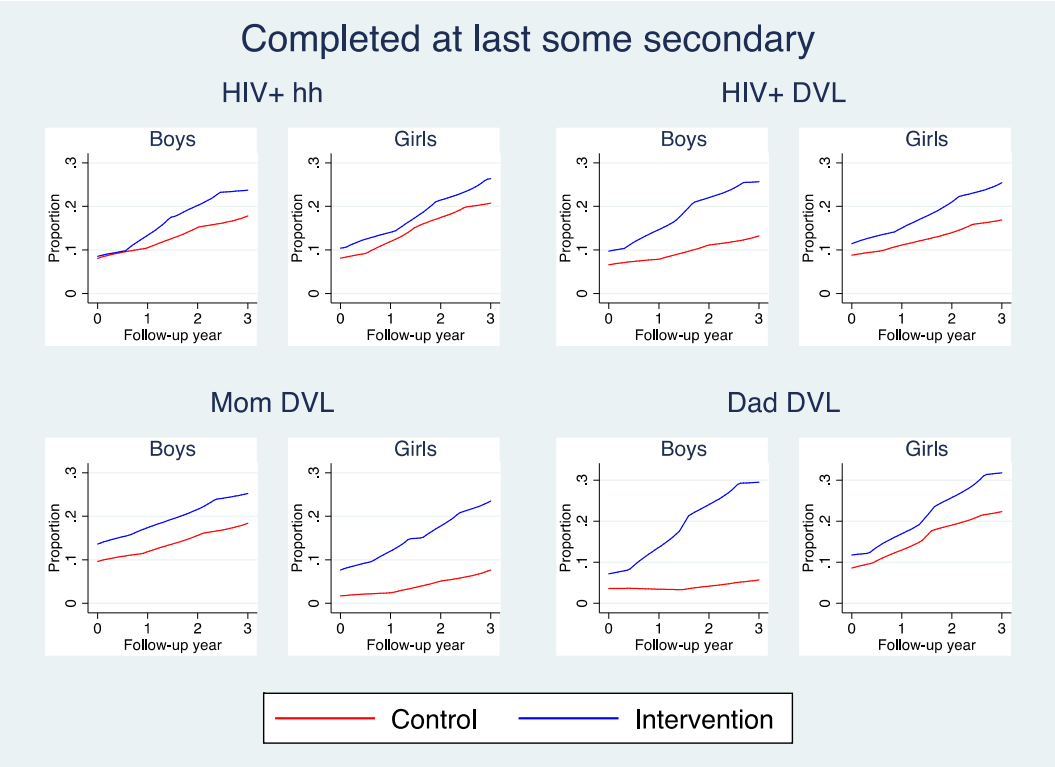

**Abbreviations:** HIV+, HIV positive; DVL, detectable viral load; FUY3, follow-up year 3
**Note:** Sample was restricted to children 9-16 years old at baseline. Dashed lines represent trends at baseline, solid lines represent trends at FUY3. Trends were estimated using nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing).

**Figure 4.2. Proportion of boys and girls 9-16 years old at baseline who completed primary school in intervention and control communities over time**



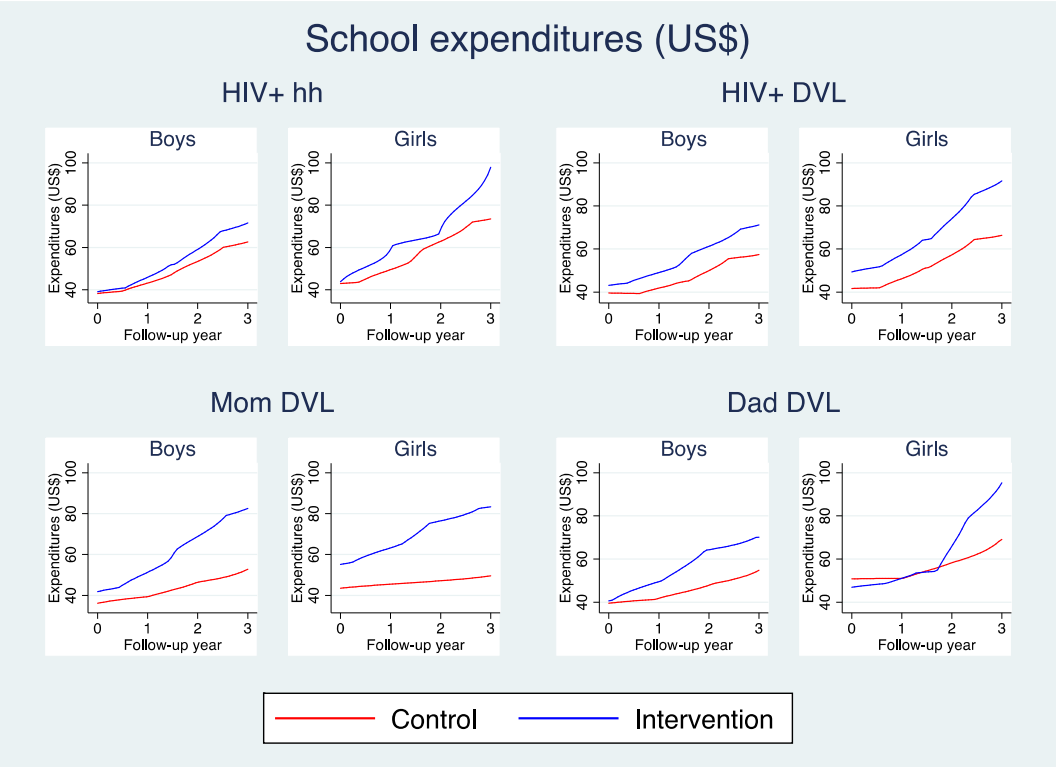

**Abbreviations:** HIV+, HIV positive; DVL, detectable viral load.
**Note:** Completion of primary school shown separately for boys and girls in intervention and control communities over time. Follow-up year 0 is the baseline. Trends were estimated using nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing).

**Figure 4.3. Proportion of boys and girls 9-16 years old at baseline who completed at least some secondary school in intervention and control communities over time**




**Abbreviations:** HIV+, HIV positive; DVL, detectable viral load.
**Note:** Completion of at least some secondary school shown separately for boys and girls in intervention and control communities over time. Follow-up year 0 is the baseline. Trends were estimated using nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing).

**Figure 4.4. Annual school expenditures in USD for boys and girls 9-16 years old at baseline in intervention and control communities over time**




**Abbreviations:** HIV+, HIV positive; DVL, detectable viral load; US$, US dollars.
**Note:** Annual school expenditures, per child, in US dollars, shown separately for boys and girls in intervention and control communities over time. Follow-up year 0 is the baseline. Trends were estimated using nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing).

**Table 4.2. Impact of SEARCH intervention on school attendance among cohort of children 9-16 years old at baseline**

| | | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Full sample | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | -0.00 | -0.00 | -0.01 | -0.01 | -0.01 | 0.00 | -0.04 | 0.07 |
| | (0.01) | (0.01) | (0.01) | (0.02) | (0.02) | (0.02) | (0.03) | (0.04) |
| Intervention * FUY2 | -0.01 | -0.02 | -0.01 | -0.00 | -0.00 | 0.00 | -0.02 | 0.03 |
| | (0.01) | (0.01) | (0.01) | (0.02) | (0.02) | (0.03) | (0.03) | (0.05) |
| Intervention * FUY3 | -0.02* | -0.02 | -0.02 | 0.01 | -0.02 | 0.02 | -0.01 | 0.07 |
| | (0.01) | (0.01) | (0.01) | (0.02) | (0.02) | (0.03) | (0.03) | (0.05) |
| Baseline mean | 0.943 | 0.953 | 0.930 | 0.924 | 0.934 | 0.935 | 0.937 | 0.931 |
| Observations | 14,374 | 8,572 | 5,802 | 2,639 | 3,862 | 1,651 | 1,010 | 641 |
| Number of id | 4,553 | 2,710 | 1,899 | 883 | 1,223 | 534 | 330 | 204 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models accounted for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 4.3. Impact of SEARCH intervention on primary school completion among cohort of children 9-16 years old at baseline**

| | | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Full sample | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 0.01 | -0.00 | 0.02 | 0.05* | 0.03 | 0.06* | 0.11** | -0.00 |
| | (0.01) | (0.01) | (0.02) | (0.02) | (0.02) | (0.03) | (0.04) | (0.05) |
| Intervention * FUY2 | 0.02 | 0.01 | 0.03 | 0.07** | 0.04 | 0.09** | 0.12** | 0.08 |
| | (0.01) | (0.01) | (0.02) | (0.02) | (0.02) | (0.03) | (0.04) | (0.05) |
| Intervention * FUY3 | 0.04** | 0.03 | 0.05** | 0.10*** | 0.06* | 0.11** | 0.13** | 0.10 |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.02) | (0.03) | (0.04) | (0.06) |
| Baseline mean | 0.0737 | 0.0739 | 0.0733 | 0.0740 | 0.0742 | 0.0728 | 0.0721 | 0.0739 |
| Observations | 14,970 | 8,906 | 6,064 | 2,757 | 4,037 | 1,723 | 1,052 | 671 |
| Number of id | 4,553 | 2,711 | 1,899 | 884 | 1,225 | 534 | 330 | 204 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 4.4. Impact of test-and-treat intervention on having at least some secondary education among cohort of children 9-16 years old at baseline**

| | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 0.01 | -0.00 | 0.02 | 0.06* | 0.03 | 0.07* | 0.10* | 0.02 |
| | (0.01) | (0.01) | (0.02) | (0.02) | (0.02) | (0.03) | (0.04) | (0.05) |
| Intervention * FUY2 | 0.03* | 0.01 | 0.05** | 0.08*** | 0.05* | 0.10** | 0.10* | 0.12* |
| | (0.01) | (0.01) | (0.02) | (0.02) | (0.02) | (0.03) | (0.04) | (0.05) |
| Intervention * FUY3 | 0.04*** | 0.03 | 0.06** | 0.11*** | 0.06* | 0.12*** | 0.13** | 0.14* |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.02) | (0.03) | (0.04) | (0.06) |
| Baseline mean | 0.0677 | 0.0702 | 0.0642 | 0.0635 | 0.0624 | 0.0574 | 0.0596 | 0.0539 |
| Observations | 14,924 | 8,878 | 6,046 | 2,752 | 4,021 | 1,720 | 1,050 | 670 |
| Number of id | 4,553 | 2,711 | 1,899 | 883 | 1,225 | 534 | 330 | 204 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 4.5. Impact of SEARCH intervention on annual school expenditures, in USD, among cohort of children 9-16 years old at baseline**

| | | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Full sample | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 7.01** | 7.55* | 6.35 | 11.60* | 10.27* | 17.68* | 19.42* | 16.38 |
| | (2.47) | (3.17) | (3.99) | (5.71) | (4.91) | (7.21) | (9.26) | (11.64) |
| Intervention * FUY2 | 6.31* | 6.28 | 6.31 | 7.41 | 10.45* | 14.89 | 17.75 | 17.42 |
| | (2.51) | (3.23) | (4.00) | (5.98) | (4.89) | (7.62) | (9.99) | (12.34) |
| Intervention * FUY3 | 9.34** | 7.49* | 11.63* | 26.74*** | 12.14* | 29.12*** | 36.06*** | 25.81 |
| | (2.87) | (3.68) | (4.64) | (6.73) | (5.62) | (8.41) | (10.71) | (13.92) |
| Baseline mean | 38.77 | 38.89 | 38.59 | 41.45 | 37.24 | 39.90 | 38.57 | 41.97 |
| Observations | 13,855 | 8,254 | 5,601 | 2,552 | 3,729 | 1,608 | 977 | 631 |
| Number of id | 4,492 | 2,671 | 1,873 | 870 | 1,207 | 528 | 325 | 203 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 4.6. Impact of test-and-treat intervention on primary school completion among cohort of children 9-16 years old at baseline, by gender**

| Panel A: Boys | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 0.02 | 0.01 | 0.04 | 0.09** | 0.06* | 0.11* | 0.12* | 0.09 |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.03) | (0.04) | (0.06) | (0.06) |
| Intervention * FUY2 | 0.04** | 0.03 | 0.07** | 0.12*** | 0.07* | 0.13** | 0.12* | 0.20** |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.03) | (0.04) | (0.06) | (0.07) |
| Intervention * FUY3 | 0.05*** | 0.05** | 0.05* | 0.13*** | 0.07* | 0.15** | 0.13* | 0.21** |
| | (0.02) | (0.02) | (0.02) | (0.04) | (0.03) | (0.05) | (0.06) | (0.07) |
| Baseline mean | 0.0670 | 0.0655 | 0.0691 | 0.0737 | 0.0689 | 0.0813 | 0.0977 | 0.0550 |
| Observations | 7,772 | 4,636 | 3,136 | 1,455 | 2,171 | 942 | 587 | 355 |
| Number of id | 2,317 | 1,374 | 968 | 456 | 657 | 290 | 180 | 110 |

| Panel B: Girls | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | -0.00 | -0.01 | 0.00 | 0.02 | -0.00 | 0.02 | 0.08 | -0.05 |
| | (0.02) | (0.02) | (0.02) | (0.04) | (0.03) | (0.05) | (0.06) | (0.08) |
| Intervention * FUY2 | 0.01 | -0.01 | 0.03 | 0.04 | 0.03 | 0.06 | 0.07 | 0.07 |
| | (0.02) | (0.02) | (0.02) | (0.04) | (0.03) | (0.05) | (0.06) | (0.08) |
| Intervention * FUY3 | 0.02 | -0.01 | 0.06* | 0.10* | 0.04 | 0.08 | 0.14* | 0.05 |
| | (0.02) | (0.02) | (0.03) | (0.04) | (0.03) | (0.05) | (0.07) | (0.09) |
| Baseline mean | 0.0806 | 0.0826 | 0.0778 | 0.0743 | 0.0802 | 0.0628 | 0.0414 | 0.0957 |
| Observations | 7,152 | 4,242 | 2,910 | 1,297 | 1,850 | 778 | 463 | 315 |
| Number of id | 2,236 | 1,337 | 931 | 427 | 568 | 244 | 150 | 94 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 4.7. Impact of test-and-treat intervention on having at least some secondary education among cohort of children 9-16 years old at baseline, by gender**

| Panel A: Boys | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 0.02 | 0.00 | 0.04 | 0.09** | 0.06* | 0.11** | 0.15** | 0.07 |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.03) | (0.04) | (0.06) | (0.07) |
| Intervention * FUY2 | 0.04** | 0.03 | 0.05* | 0.11*** | 0.06* | 0.13** | 0.14* | 0.15* |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.03) | (0.04) | (0.06) | (0.07) |
| Intervention * FUY3 | 0.05*** | 0.06** | 0.06* | 0.13*** | 0.07* | 0.15** | 0.14* | 0.17* |
| | (0.02) | (0.02) | (0.02) | (0.04) | (0.03) | (0.05) | (0.06) | (0.08) |
| Baseline mean | 0.0626 | 0.0640 | 0.0607 | 0.0601 | 0.0578 | 0.0634 | 0.0805 | 0.0364 |
| Observations | 7,792 | 4,646 | 3,146 | 1,458 | 2,181 | 945 | 589 | 356 |
| Number of id | 2,317 | 1,374 | 968 | 456 | 657 | 290 | 180 | 110 |

| Panel B: Girls | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | -0.01 | -0.01 | -0.01 | 0.01 | -0.01 | 0.00 | 0.06 | -0.07 |
| | (0.02) | (0.02) | (0.02) | (0.04) | (0.03) | (0.04) | (0.06) | (0.08) |
| Intervention * FUY2 | -0.00 | -0.01 | 0.01 | 0.03 | 0.02 | 0.05 | 0.09 | 0.02 |
| | (0.02) | (0.02) | (0.02) | (0.04) | (0.03) | (0.05) | (0.06) | (0.08) |
| Intervention * FUY3 | 0.02 | -0.01 | 0.05 | 0.06 | 0.03 | 0.07 | 0.15* | 0.01 |
| | (0.02) | (0.02) | (0.03) | (0.04) | (0.04) | (0.05) | (0.06) | (0.09) |
| Baseline mean | 0.073 | 0.0765 | 0.0678 | 0.0671 | 0.0677 | 0.0502 | 0.0345 | 0.0745 |
| Observations | 7,178 | 4,260 | 2,918 | 1,299 | 1,856 | 778 | 463 | 315 |
| Number of id | 2,236 | 1,337 | 931 | 428 | 568 | 244 | 150 | 94 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Table 4.8. Impact of test-and-treat intervention on school expenditures (in USD) among cohort of children 9-16 years old at baseline, by gender**

| Panel A: Boys | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 9.02** | 10.22* | 6.47 | 15.15* | 11.53 | 22.51* | 27.59* | 12.40 |
| | (3.28) | (4.14) | (5.38) | (7.49) | (6.43) | (9.08) | (11.69) | (14.50) |
| Intervention * FUY2 | 8.02* | 6.46 | 9.94 | 4.05 | 16.57** | 16.82 | 13.68 | 30.41 |
| | (3.32) | (4.22) | (5.41) | (7.93) | (6.40) | (9.67) | (12.71) | (16.02) |
| Intervention * FUY3 | 7.44* | 5.57 | 8.99 | 17.81* | 11.43 | 24.47* | 38.70** | -0.06 |
| | (3.75) | (4.74) | (6.22) | (8.84) | (7.26) | (10.56) | (13.56) | (17.07) |
| Baseline mean | 36.16 | 36.45 | 35.74 | 39.60 | 32.21 | 35.56 | 35.47 | 35.70 |
| Observations | 7,200 | 4,314 | 2,886 | 1,346 | 2,000 | 873 | 538 | 335 |
| Number of id | 2,288 | 1,357 | 955 | 452 | 646 | 287 | 178 | 109 |

| Panel B: Girls | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 4.87 | 4.93 | 6.02 | 7.41 | 8.90 | 13.66 | 14.94 | 16.07 |
| | (3.74) | (4.86) | (5.94) | (8.79) | (7.57) | (11.75) | (15.05) | (18.59) |
| Intervention * FUY2 | 4.61 | 6.42 | 2.45 | 11.72 | 3.70 | 14.42 | 23.35 | 11.22 |
| | (3.80) | (4.97) | (5.96) | (9.10) | (7.55) | (12.32) | (16.21) | (19.40) |
| Intervention * FUY3 | 11.05* | 9.41 | 13.45 | 32.53** | 12.73 | 31.04* | 30.93 | 44.82 |
| | (4.41) | (5.74) | (6.97) | (10.41) | (8.82) | (13.97) | (17.97) | (23.21) |
| Baseline mean | 41.50 | 41.44 | 41.58 | 43.43 | 43.04 | 44.94 | 42.15 | 49.28 |
| Observations | 6,655 | 3,940 | 2,715 | 1,206 | 1,729 | 735 | 439 | 296 |
| Number of id | 2,204 | 1,314 | 918 | 418 | 561 | 241 | 147 | 94 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

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# CHAPTER 5: CONCLUSIONS

## 5.1 Summary and synthesis of findings

The overarching goal of this dissertation was to use population-representative data and rigorous empirical methods to identify the effect of large-scale, disease-specific interventions on health and economic outcomes. To my knowledge, this was the first study to assess the association between PMI and all-cause child mortality in sub-Saharan Africa using appropriate comparison groups and adjustments for regional trends in child mortality. This was also the first study to assess economic outcomes of HIV-positive individuals over a wide range of disease stages as well as the socio-economic outcomes of their household members, including evidence about the potential economic gains of finding and treating persons with HIV early in their disease course. Finally, this was the first study to provide causal evidence about the effect of HIV test-and-treat on investments in human capital. The dissertation relied on population-representative data, which improved our ability to generalize the study findings to other countries in SSA. The results provide rigorous and objective evidence that programs such as PMI and PEPFAR offer substantial returns on investment in the form of reduced mortality, improved economic functioning, and higher investments in human capital.

In Chapter 2, I used a quasi-experimental technique to evaluate child mortality trends in PMI-recipient versus comparison countries, before and after implementation of the program. I leveraged data from multiple publicly-available sources to assess child mortality trends in 32 countries in SSA spanning a period that included about ten years before and ten years after the introduction of the program. The main study finding was that the introduction of PMI was

associated with a 16% reduction in the annual risk of all-cause mortality among children aged <5 years. This finding was confirmed using a measure of annual per-capita PMI disbursements to recipient countries. In other words, following the introduction of PMI, the pace of child mortality decline accelerated significantly in the recipient countries. Our model accounted for the overall trends in child mortality in Africa, the baseline differences in child mortality rates between study countries, availability of other funding sources including the Global Fund and PEPFAR, and various individual-level and household-level covariates.

Moreover, at the same time as child mortality was decreasing, population coverage of the key malaria prevention and treatment interventions funded by PMI was increasing. On average, introduction of PMI was associated with 8.3 percentage points increase in ITN coverage increased by, 6.6 percentage points increase in IRS coverage, and 3.6 percentage points increase in ACT coverage. The association between PMI and all our study outcomes grew larger in magnitude over time. Finally, our robustness checks showed that the association between PMI and child mortality was even larger in rural areas, where malaria burden is generally greater, and was larger in magnitude when we excluded deaths that occurred within first month of a child's life (i.e. deaths that would have been avoided more likely due to prenatal or delivery care than PMI efforts). In sum, PMI significantly contributed to reducing the burden of malaria and the number of child deaths in SSA.

In Chapter 3, I used baseline data from SEARCH, a large, population-representative HIV test-and-treat trial conducted in 32 communities in Kenya and Uganda. The main goal of this analysis was to explore the economic functioning of HIV-positive people who have high CD4+ T-cell counts (i.e. people who are not yet symptomatic). According to historical WHO guidelines, HIV-positive people in low-resource settings had to await treatment initiation until

their CD4+ counts declined below a certain threshold. As such, previous studies have documented an individual-level decline in employment outcomes among HIV-positive people who awaited treatment initiation, followed by a rebound in economic outcomes after ART initiation at the low CD4 count threshold. However, studies that assess outcomes of asymptomatic, high CD4+ adults are lacking. In this cross-sectional study, several economic outcomes of HIV-positive individuals with high CD4 were assessed and contrasted to those of other HIV-positive and HIV-negative individuals. Furthermore, unlike many prior studies of adults initiating ART and population-based studies of HIV, our study included data on key health indicators such as the CD4+ T-cell count and HIV RNA and offered a more generalizable depiction of the association between CD4 counts and economic outcomes in the general population.

The findings from the baseline SEARCH study are consistent with the hypothesis that population level HIV testing and early ART initiation may help avert an economic decline associated with HIV disease progression. We found that economic outcomes of HIV-positive individuals with high CD4 counts (i.e. >500 cells/mL) were significantly better than those for HIV-positive individuals with CD4≤500 and were comparable to outcomes for HIV-negative participants. Furthermore, high CD4 count of the HIV-positive household member was similarly protective of employment outcomes for HIV-negative household members of the HIV-positive persons. Patterns in healthcare utilization and healthcare costs incurred by HIV-positive individuals also indicated a benefit to having higher CD4 counts, even though the outcomes of those with high CD4 remained poorer than those for HIV-negative persons in households not directly affected by HIV. Importantly, even among HIV-positive participants who had not initiated ART or were not virally suppressed, those with high CD4 had better economic

outcomes than those with lower CD4 counts, including people in the mid-range of 351-500 cells/μL. This suggests that initiating ART before CD4 counts decline below 500 cells could generate economic benefits.

In Chapter 4, I used longitudinal data from the SEARCH trial to evaluate the impact of HIV test-and-treat intervention on investments in human capital. I constructed a cohort of HIV-negative children who were 9-16 years old at baseline, a critical age range for achieving the major milestones of completing primary education and entering secondary education, and compared education outcomes of these children in the intervention communities versus control communities during three years of follow-up. Children were categorized into study groups based on the HIV status and viral load suppression status of adults in their households. I focused on households with HIV-positive adults who had detectable viral load (i.e. were in need of ART) and I also examined children whose biological parent had HIV and detectable viral load.

Children in the intervention communities had significantly higher probability of completing primary school and having at least some secondary school education than children in control communities. I examined the effect of the intervention among all children in the intervention communities and by sub-groups. This design enabled me to conclude that children who benefitted the most from the intervention were those who resided with an adult who had HIV and who was in need in treatment at baseline, especially if that adult was the biological parent. I also found that the average annual school expenditures per child increased quite significantly in the intervention communities, particularly among children whose mothers had detectable viral loads, compared to their counterparts in control communities. The study findings suggest that investments in test-and-treat could have multigenerational spillover effects with implications for economic development in low-income countries.

In summary, each study aim provided evidence about the various benefits of health interventions in sub-Saharan Africa that are funded with US dollars. Results from this study fill important gaps in literature and use innovative study designs that attempt to limit sources of potential bias. My dissertation also demonstrates innovative use of publicly-available data to evaluate the impact of large-scale health policies on population health. Furthermore, evidence from the SEARCH trial exemplifies the value of collecting economic data as part of controlled trials testing the impact of health interventions. The overarching findings from this dissertation underline the close links that exists between health status, earning potential, and the ability to invest in future generations.

### 5.1.1 Policy implications

This study was designed primarily to inform public policy debate. My goal was to provide meaningful and objective evidence to policy makers about the potential returns on investment in large-scale health interventions. The study findings indicate that health investments in SSA have produced large returns in terms of lower child mortality, improved economic functioning of working-age adults, and higher investments in children's education. These health and economic gains have significant implications for economic growth of populations that live in areas where the burden of infectious diseases remains high. At a time when the value of humanitarian aid is being questioned, I provide clear evidence that investments in health interventions have positive spillover effects to other sectors and may ultimately strengthen the economic development of nations in the sub-Saharan region.

Among some of the key study findings that could help guide policy debate about future funding levels are the following results. First, this study showed that PMI was associated with large and meaningful reductions in child mortality. In other words, PMI's investment in evidence-based malaria interventions appears to have provided large positive returns in terms of

reduced malaria burden and lower child mortality. Second, using baseline data from a randomized trial of HIV test and treat, the study documented suggestive evidence that maintaining high CD4 counts of HIV-positive adults may have positive economic impact on the individuals starting ART early, as well as their household members. Furthermore, using longitudinal data, I found that HIV test-and-treat intervention led to higher investments in children's education. Expanded access to HIV testing and treatment in sub-Saharan Africa relies in large part on continued partnership of PEFPAR with the recipient governments. At a time of increasing uncertainty about future funding levels of US foreign aid, this study provides objective evidence that programs such as PMI and PEFPAR offer substantial returns on investment.

The new US administration has proposed large cuts to US foreign aid funding in its 2018 budget proposal, citing low value of sending health aid to low-income countries. Evidence from this study provides evidence about the large and meaningful returns on investments in health aid. Aside from the clear humanitarian value of health interventions, large-scale health programs may also offer other benefits in terms of economic development and improved perception of the US abroad. For example, stronger economic partners in Africa may provide new and exciting trade opportunities for the US, which may of particular interest to the current US administration. According to a Perspective, written by Dr. Eran Bendavid, that accompanied our PMI paper in PLOS Medicine, perceptions of the United States are highly favorable in some of the countries that have partnered with PMI and PEPFAR. This may be, at least in some part, due to the United States' role in bringing life-saving prevention and treatment health interventions to the populations of those countries. PEPFAR and PMI are two large-scale programs that are highly visible and successful in Africa. The success of these programs in recipient countries promotes

the United Sates as a leader and champion of global health, especially in the fight against HIV/AIDS and malaria. In sum, this study provides evidence about the returns on investments in global health interventions that extend beyond the health sector. The US Congress and administration should consider evidence from this study as they deliberate future funding levels of foreign aid.

### 5.2 Limitations and Future Directions

This study was subject to several limitations. First, the difference-in-differences technique used to evaluate PMI relied on the assumption that there were no important unmeasured variables that differentially affected mortality rates in PMI and comparison countries during the study period. We used country fixed effects to control for all time-invariant differences between countries and year fixed effects to control for the underlying time trends in the region. Yet our study could still suffer from omission of important time-varying characteristics, which could bias our study results if the omitted variables affected PMI and comparison countries in different ways. For this reason, we cannot definitively interpret these results from this analysis as causal. Given the large-scale nature of the PMI program and the fact that the program was not implemented as a randomized experiment, we believe that our careful study design was the most robust way of measuring the role PMI has played in curbing child mortality in SSA.

While the PMI analysis incorporated data from multiple sources, we could not find several important indicators that would have strengthened our study design. For example, we were not able to account for national government spending on malaria interventions due to lack of reliable data. Future studies that include countries' own contributions to fighting malaria could provide a fuller picture of which sources of funding for malaria interventions offer the highest value for money. We also lacked data on rapid diagnostic testing and intermittent-prevention

therapy during pregnancy, both of which could have contributed to lowering malaria burden in PMI countries. According to internal PMI reports, coverage of IPTp (2 doses of sulfadoxine-pyrimethamine) increased in PMI countries from 14% at baseline to 38% in 2015. However, I was not able to assess whether these increases are on par with or above the average trends in the rest of SSA. Future research should explore the potential impact of PMI on health behaviors in households with pregnant women.

Economic theory suggests that the lower burden of malaria disease due to PMI-supported interventions may translate to reduced household financial burdens associated with caring for ill household members and lost wages, improved life-expectations, and less strain on health systems associated with treating malaria cases. In other words, the health gains from PMI investment may have spillover effects beyond health, such as higher school attainment and labor productivity, which might in turn lead to greater economic development. Future research should explore whether investments made through programs such as PMI did in fact improve education and economic outcomes in SSA.

The analysis of HIV disease progression and economic outcomes relied on cross-sectional data, which precluded us from assessing the causal impact of declining health status of HIV-positive people on economic outcomes. Nonetheless, we believe that the study findings provide meaningful insights about the association between HIV disease and economic outcomes. The SEARCH household socio-economic survey collected a wealth of data on the economic functioning of study participants. These data relied on recall and accuracy of responses of the study respondent, usually the household head. We attempted to limit the biases common to survey data by using short recall periods that are common in similar literature. Moreover, the main indicators of health status were laboratory-confirmed measures of HIV status and CD4

counts. The use of objective measures of health represents an advance in comparison to other studies of the link between health and economic outcomes that relied on self-reported health status.

The education analysis relied on measurement of major milestones reached by children, such as completion of primary school, completion of at least some secondary school, and annual school expenditures. Yet schools in low-resource settings are notorious for providing poor quality of education to children, which complicates conclusions about whether attending more school necessarily translates to better education. Future research should include more detailed data about the quality of children's education, including measures of literacy, math skills, and cognitive development. Such data would inform future research about the important question of whether higher school attainment and expenditures in the test-and-treat intervention communities also translated to better quality of education.

### 5.3 Conclusion

The analyses included in this dissertation provided important insights about the value of bringing life-saving prevention and treatment interventions to populations in low-resource settings. We found that implementation of the health interventions supported with US funding was associated with lower burden of disease in the recipient populations, improved economic functioning of adults, and has led to higher investments in future generations. The study findings point to important spillover effects of health interventions to other sectors, which could eventually lead to improved economic development of countries in SSA. The analyses completed as part of this dissertation offer objective evidence about the potential returns on investments in global health aid. The study findings should be considered by the United States administration and Congress as they deliberate future funding levels for bilateral aid programs such as PMI and PEPFAR.

# APPENDIX 1: CHAPTER 2 SUPPLEMENTAL MATERIALS

## Supplemental materials table of contents

## Description of Sample and Exposure

The US President's Malaria Initiative (PMI) began as a small program in 2006 with funding directed to three countries (Angola, Tanzania and Uganda) and an annual budget of $30 million. By 2011, PMI had expanded to 19 countries in SSA (Angola, Benin, Democratic Republic of Congo, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Tanzania, Uganda, Zambia, and Zimbabwe) and had an annual budget of approximately $600 million [1]. Our sample included all 19 PMI countries and 13 PMI comparison countries (Burkina Faso, Burundi, Cameroon, Chad, Congo, Cote d'Ivoire, Gabon, Namibia, Niger, Sierra Leone, Swaziland, The Gambia, and Togo). We excluded from the analysis malaria non-endemic countries (Lesotho), small island countries (Comoros, Sao Tome and Principe) and South Africa, since only one DHS from 1998 was available there. Appendix 1 Table A includes detailed information about when PMI started operating in each country and when other large funding sources, namely the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) and the US President's Emergency Plan for AIDS Relief (PEPFAR), began operating in the study countries.

## Data Sources

***Child mortality data***

Data on child mortality were extracted from every Demographic and Health Surveys (DHS) and Malaria Indicator Surveys (MIS) and AIDS Indicator Surveys (AIS) conducted between 1995 to 2014 that included child's year and month of birth and age at death (in months). The DHS, MIS and AIS are standardized surveys collected by ICF International and funded by USAID that provide nationally-representative data on health and population in developing countries. Surveys were typically conducted every 5 years using standardized questionnaires with the goal of allowing for comparisons across countries and time. While some parts of the questionnaire have evolved over time, a core set of questions appeared in each data collection tool: household characteristics, woman characteristics, pregnancy/birth history. The child mortality data used in this study were obtained from birth history modules extracted from 77 DHS and 14 MIS and 5 AIS conducted between 1995 and 2014 [2].

DHS, MIS and AIS households were selected for participation in the survey using a 2-stage sampling design, where representative clusters were first selected from a national sampling frame and a random sample of households was then selected from within each cluster. Each survey thus yields a nationally-representative sample of households. In each sampled household, all women between 15 and 49 years old who were stable residents of the households were interviewed. Sampled women were asked detailed background characteristics and information on antenatal and postnatal care, place of delivery, who attended the delivery, birth weight, and the nature of complications during pregnancy for recent births. Women were also asked whether the child she gave birth to was still alive, and if not, when the child died.

We constructed a longitudinal cohort with repeated observations for each child who was <5 years of age between 1995 and 2014. We used information about whether each child was alive or dead, the year of child's birth, and how old a child was when s/he died, when applicable, to create binary indicators of whether a child was deceased in each year. That is, we began with a set of women $W_{mjt}$ sampled in country $j$ and year $t$. We then restricted the sample to women who had ever given birth to a child and used information on child $i$ date of birth to determine whether child $i$ was between the ages of 0 and 5 years during study period (1995-2014), dropping all children older than 5 years old from the analysis. The three numbers $i, j, t$ uniquely identified each child in each survey. For each eligible (<5 years) child $i$ in our data we then generated a sequence of binary variables that indicated whether a child died in a given calendar year $t$. Our primary analytic dataset consisted of this sequence of binary variables, along with country characteristics for each year $t$, and all other characteristics that we knew about the child, mother and

household from the index woman's $W_{mjt}$ survey responses (the child's age and gender, mother's age, mother's education level, mother's parity, household wealth, household was located in rural area, and whether female was the head of household). Appendix 1 Table A lists the number of child-year observations available per country, the number of unique children in our datasets and the number of deaths reported in each country. This analytic plan was similar to that used in other studies that have evaluated large-scale programs [3, 4].

## Appendix 1 Table A. Year of program implementation, year of DHS survey collection, and sample description

| | Year Program Initiated | | | Sample Description | | | |
|---|---|---|---|---|---|---|---|
| | PMI | PEPFAR | Global Fund | Interview years | Number of child-year observations | Number of unique children | Number of deaths |
| PMI Countries | | | | | | | |
| Angola | 2006 | 2007 | 2005 | 2006-07, 2011 | 86,331 | 22,596 | 1,796 |
| Benin | 2008 | | 2003 | 1996, 2001, 2006, 2011-12 | 370,331 | 102,199 | 8,077 |
| Congo, DRC | 2011 | 2007 | 2003 | 2007, 2013-14 | 295,437 | 77,322 | 8,295 |
| Ethiopia | 2008 | 2004 | 2003 | 2000, 2005, 2011 | 308,402 | 86,366 | 8,393 |
| Ghana | 2008 | 2007 | 2003 | 1998-99, 2003, 2008, 2014 | 164,164 | 44,705 | 3,169 |
| Guinea | 2011 | | 2003 | 1999, 2005, 2012 | 184,426 | 52,235 | 5,997 |
| Kenya | 2008 | 2004 | 2003 | 1998, 2003, 2008-09, 2014 | 456,484 | 117,494 | 6,677 |
| Liberia | 2008 | | 2004 | 2006-07, 2008-09, 2011, 2013 | 216,059 | 57,743 | 6,418 |
| Madagascar | 2008 | | 2003 | 2003-04, 2008-09, 2011, 2013 | 245,162 | 66,524 | 3,410 |
| Malawi | 2007 | 2006 | 2003 | 2000, 2004-05, 2010, 2012, 2014 | 389,551 | 110,644 | 11,096 |
| Mali | 2008 | | 2003 | 2001, 2006, 2012-13 | 337,077 | 95,958 | 12,035 |
| Mozambique | 2007 | 2004 | 2004 | 2003-04, 2011 | 201,349 | 55,698 | 5,900 |
| Nigeria | 2011 | 2004 | 2003 | 2003, 2008, 2010, 2013 | 815,253 | 216,519 | 27,219 |
| Rwanda | 2007 | 2004 | 2003 | 2000, 2005, 2010-11, 2013 | 234,697 | 66,684 | 6,717 |
| Senegal | 2007 | | 2003 | 2005, 2008-09, 2010-11, 2012-13, 2014 | 568,322 | 149,602 | 12,714 |
| Tanzania | 2006 | 2004 | 2003 | 1999, 2004-05, 2007-8, 2009-10, 2011-12 | 291,498 | 81,687 | 5,643 |
| Uganda | 2006 | 2004 | 2003 | 2000-01, 2006, 2009-10, 2011 | 259,828 | 71,668 | 6,545 |
| Zambia | 2008 | 2004 | 2003 | 2001-02, 2007, 2013-14 | 285,167 | 75,298 | 6,621 |
| Zimbabwe | 2011 | 2006 | 2003 | 1999, 2005-06, 2010-11 | 128,460 | 35,882 | 1,829 |
| Comparison Countries | | | | | | | |
| Burkina Faso | | | 2003 | 1998-99, 2003, 2010, 2014 | 307,002 | 88,099 | 9,308 |
| Burundi | | 2011 | 2003 | 2010-11, 2012-13 | 98,434 | 26,528 | 2,210 |
| Cameroon | | 2011 | 2004 | 1998, 2004, 2011 | 218,262 | 61,086 | 5,522 |
| Chad | | | 2004 | 2004 | 47,646 | 13,931 | 1,771 |
| Congo | | | 2006 | 2005, 2011-12 | 147,884 | 39,342 | 3,001 |
| Côte d'Ivoire | | 2004 | 2003 | 1998-99, 2011-12 | 103,514 | 27,894 | 2,902 |
| Gabon | | | 2004 | 2000-01, 2012 | 101,572 | 27,897 | 1,428 |
| Namibia | | 2004 | 2004 | 2000, 2006-07, 2013 | 143,678 | 38,993 | 1,805 |
| Niger | | | 2004 | 1998, 2006, 2012 | 272,762 | 76,280 | 9,611 |
| Sierra Leone | | | 2003 | 2008, 2013 | 225,477 | 59,209 | 8,755 |
| Swaziland | | 2007 | 2003 | 2006-07 | 28,425 | 7,838 | 572 |
| The Gambia | | | 2004 | 2013 | 96,713 | 24,370 | 1,397 |
| Togo | | | 2003 | 1998, 2013-14 | 122,704 | 34,660 | 2,648 |

**Abbreviations:** PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.

***Malaria prevention and treatment technology coverage***

We obtained data about population-level utilization of key malaria prevention and treatment interventions in sub-Saharan Africa from the Malaria Atlas Project (MAP), a non-profit organization at Oxford University, funded primarily by the Bill and Melinda Gates Foundation. The chief objective of MAP was to disseminate free, accurate and up-to date data on malaria and associated topics, organized on a geographical basis [5]. Coverage data from over one million households were combined with national malaria control program data on ITN, ACT and IRS provision to develop time-series models of coverage of these interventions within each country. Data sources included the Demographic Health Surveys (DHS), Malaria Indicator Surveys (MIS), Multiple Cluster Surveys (MICS), AIDS Indicator Surveys (AIS), Malaria and Anemia Prevalence Survey (EA & P), and the World Health Organization (WHO) [5].

The unit of analysis of MAP data was at the country-year level. ITN estimate represented the proportion of people who slept under an insecticide-treated bednet on any given night; ACTs estimate represented the proportion of fever cases in under-5 year olds that were treated with artemisinin-based combination therapy; IRS estimate represented the proportion of the population protected by indoor residual spraying of insecticides.

***Program activity data***

We extracted data about years when PMI began operations in each of the study countries from the PMI's Tenth Annual Report to Congress (2016) [6]. Our study design accounted for the gradual enrollment of countries to receive PMI funding and for the fact that other large funding sources were present in the recipient countries during the study period. That is, we created an indicator for PMI program based on the actual year when funds were first disbursed, thus taking advantage of the variation in program rollout in the sample. We used the same strategy to create indicators for whether countries in the sample received PEPFAR and GFATM aid using publically-available government documents about program implementation [6-8].

The binary indicator of PMI program activity did not take into account that disbursement levels vary between countries and even within countries over time. In order to address this, we used data about the annual level of funds disbursed to each country to create a measure of program scope and intensity. These data were extracted from publically-available Development Assistance for Health 1990-2014 database developed by the Institute for Health Metrics and Evaluation (IHME) in Seattle WA [9]. IHME collected data from organizations that provided health-related funding in developing countries from 1990 through 2012. The dataset distinguished between the funding source (or country of origin), the channel through which funds were distributed (bilateral vs. multilateral vs. private foundations), health focus area (e.g. malaria, HIV) and where the funds were disbursed (or recipient country). This data structure enabled us to divide the development assistance for health to sub-Saharan Africa into six categories of interest.

The process to calculate per-capita disbursements was as follows: 1) we extracted the PMI disbursements in each country and year by summing all disbursements allocated to malaria interventions from the United States government through bilateral agreements; 2) we extracted funds from the Global Fund that were allocated specifically to malaria interventions; 3) we then grouped the remaining malaria aid from all other sources and channels into "other malaria aid" category; 4) we grouped Global Fund disbursements for HIV and tuberculosis; 5) we extracted PEPFAR disbursements by summing the funds allocated to HIV/AIDS interventions from the United States government through bilateral channels; and 6) we grouped all remaining development assistance for health into "other health aid" category. These six funding channels summed to 100% of health aid included in the IHME database as having provided funding to sub-Saharan Africa during the study period. In a final step we divided the disbursements in each of the six categories by the total country population in a given year, which we obtained from the World Development Indicators database [10]. Thus, the indicators that were included in the analysis represented per-capita development assistance for health in 2014 US dollars.

## Statistical Analysis

***Child mortality models***

First, we evaluated the association between PMI and all cause under-5 mortality by fitting modified Poisson regression models specified in Models (1-3):

$$(1)\ Y_{ijt} = \alpha_j + \beta\, POST_{jt} * PMI_j + \gamma_t + \varepsilon_{ijt}$$
$$(2)\ Y_{ijt} = \alpha_j + \beta\, POST_{jt} * PMI_j + \mu\, POST_{jt} * GF_j + \eta\, POST_{jt} * PEPFAR_j + \gamma_t + \varepsilon_{ijt}$$
$$(3)\ Y_{ijt} = \alpha_j + \beta\, POST_{jt} * PMI_j + \mu\, POST_{jt} * GF_j + \eta\, POST_{jt} * PEPFAR_j + \lambda\, Z_{ijt} + \gamma_t + \varepsilon_{ijt}$$

where $Y_{ijt}$ was the outcome variable set to 1 if a child *i* from country *j* in year *t* died and 0 otherwise. $POST_{jt}*PMI_j$ variable was set to 1 if child *i* resided in country *j* that received PMI funds in year *t.* $POST_{jt}*GF_j$ was set to 1 if child *i* resided in country *j* that received Global Fund aid in year *t.* $POST_{jt}*PEPFAR_j$ was set to 1 if child *i* resided in country *j* that received PEPFAR funds in year *t.* $POST_{jt}*GF_j$ and $POST_{jt}*PEPFAR_j$ variables, which were added in Model (2), improved identification of PMI program by adjusting for the presence of other large funding sources to the region. $Z_{ijt}$ *was* a vector of descriptive characteristics that was added in Model (3): child's age (binary indicators for each year of child's life), child's gender (binary indicator for female), mother's age (continuous measure of age), mother's education (binary indicators for no education, primary education, and secondary of higher education), mother's parity (continuous measure of the number of births given by the mother), urban/rural setting (binary indicator for rural), wealth index (binary indicators for wealth quintile of the household). Less than 5% of the study sample had missing data on household-level variable of wealth. We ran regression models using complete case analysis, i.e. observations with missing data were not used in the analysis. $\alpha_j$ *was* a full set of country dummies to control for baseline country characteristics, and $\gamma_t$ was a full set of year dummies to account for secular trends.

The coefficients of interest in Models (1-3) were $\beta$*'s*, which represented the difference-in-differences estimate of the PMI program, or the average annual change in risk of all-cause under-5 mortality in PMI countries. The exponentiated coefficient from Modified Poisson regression (i.e., Poisson regression with a robust error variance) provides a measure of relative risk [11, 12]. Standard errors were clustered at the country level to relax the assumption of independently and identically distributed error terms within countries [13].

Second, we evaluated the association between PMI program intensity and all-cause under-5 mortality by fitting modified Poisson regression models specified in Models (4-6):

$$(4)\ Y_{ijt} = \alpha_j + \delta\, PC\_PMI\_aid_{jt} + \gamma_t + \varepsilon_{ijt}$$
$$(5)\ Y_{ijt} = \alpha_j + \delta\, PC\_PMI\_aid_{jt} + \phi\, PC\_GF\_MALARIA\_aid_{jt} + \mu\, PC\_OTHER\_MALARIA\_aid_{jt} + \eta\, PC\_GF\_HIV\_TB\_aid_{jt} + \theta\, PC\_PEPFAR\_aid_{jt} + \rho\, PC\_ALL\_OTHERaid_{jt} + \gamma_t + \varepsilon_{ijt}$$
$$(6)\ Y_{ijt} = \alpha_j + \delta\, PC\_PMI\_aid_{jt} + \phi\, PC\_GF\_MALARIA\_aid_{jt} + \mu\, PC\_OTHER\_MALARIA\_aid_{jt} + \eta\, PC\_GF\_HIV\_TB\_aid_{jt} + \theta\, PC\_PEPFAR\_aid_{jt} + \rho\, PC\_ALL\_OTHERaid_{jt} + \lambda\, Z_{ijt} + \gamma_t + \varepsilon_{ijt}$$

where $Y_{ijt}$ was the outcome variable set to 1 if a child *i* from country *j* in year *t* died and 0 otherwise. We began with Model 4 which only included the $PC\_PMI\_aid_{jt}$ variable, a continuous measure of the amount of aid disbursed through PMI in country *j* in year *t.* In Model (5) we added other continuous measures of per-capita spending to account for the presence and scale of other large-scale donors in the study countries. $PC\_GF\_MALARIA\_aid_{jtI}$ variable measured the amount of aid from the Global Fund that was allocated towards malaria interventions in country *j* in year *t.* $PC\_OTHER\_MALARIA\_aid_{jt}$ variable measured the amount of aid from all other sources allocated toward malaria interventions in country *j* in year *t.* $PC\_GF\_HIV\_TB\_aid_{jt}$ variable measured the amount of aid from the Global Fund that was

allocated towards HIV and tuberculosis interventions in country *j* in year *t*. $PC\_PEPFAR\_aid_{jt}$ variable measured the amount of aid from the PEPFAR disbursed in country *j* in year *t*. $PC\_ALL\_OTHERaid_{jt}$ variable measured all other aid disbursed in country *j* in year *t*. All per-capita variables were continuous measures of aid in constant 2014 US dollars. Finally, in Model (6) we added $Z_{ijt}$ , a vector of descriptive characteristics: child's age (binary indicators for each year of child's life), child's gender (binary indicator for female), mother's age (continuous measure of age), mother's education (binary indicators for no education, primary education, and secondary of higher education), mother's parity (continuous measure of the number of births given by the mother), urban/rural setting (binary indicator for rural), wealth index (binary indicators for wealth quintile of the household). $\alpha_j$ *was* a full set of country dummies to control for baseline country characteristics and $\gamma_t$ was a full set of year dummies to account for secular trends.

The coefficients of interest in Model (4-6) were $\delta$*'s*, which measured the average annual change in risk of all-cause under-5 mortality as a function of an additional per-capita PMI aid spent annually. The exponentiated coefficient from Modified Poisson regression provides a measure of relative risk. Robust standard errors were clustered at the country level to relax the assumption of independently and identically distributed error terms [13]. The other PC measures were included to help improve identification of PMI program activity by controlling for health aid disbursed through other channels in the same study countries and years, and individual-level characteristics were added to account for child's, mother's, and household characteristics that might have affected child's risk of mortality.

***Malaria interventions models***

Third, we evaluated the association between PMI and population coverage of ITNs, ACTs, and IRS by fitting ordinary least squares (OLS) regression models specified in Model (7):

$$(7)\ Y_{jt} = \alpha_j + \lambda\, POST_{jt} * PMI_j + \mu\, POST_{jt} * GF_j + \eta\, POST_{jt} * PEPFAR_j + \pi\, population\_size_{jt} + \gamma_t + \varepsilon_{jt}$$

where $Y_{jt}$ were country-level continuous outcome variables: 1) percentage of population who slept under ITN on any given night; 2) percentage of cases of fever in under-5 year olds that were treated with ACT and 3) percentage of population protected by indoor residual spraying of insecticides. $POST_{jt} * PMI_j$, $POST_{jt} * GF_j$ and $POST_{jt} * PEPFAR_j$ variables were specified as discussed above. $Population\_size_{jt}$ was a time-varying continuous measure of population size in country *j* in year *t*. $\alpha_j$ was a full set of country dummies to control for baseline country characteristics and $\gamma_t$ was a full set of year dummies to account for secular trends.

The coefficient of interest in Model (7) was $\lambda$, which represented the average annual percentage change in ITNs, ACTs and IRS coverage after implementation of PMI. Robust standard errors were calculated to correct for potential heteroskedasticity of the error term.

Fourth, we evaluated the association between PMI program intensity and population coverage of ITNs, ACTs and IRS by fitting ordinary least squares (OLS) regression model specified in Model (8):

$$(8)\ Y_{jt} = \mu\, PC\_PMI\_aid_{jt} + \phi\, PC\_GF\_MALARIA\_aid_{jt} + \nu\, PC\_OTHER\_MALARIA\_aid_{jt} + \eta\, PC\_GF\_HIV\_TB\_aid_{jt} + \theta\, PC\_PEPFAR\_aid_{jt} + \rho\, PC\_ALL\_OTHERaid_{jt} + \pi\, population\_size_{jt} + \gamma_t + \varepsilon_{ijt}$$

where $Y_{jt}$ were country-level continuous outcome variables of population coverage of ITNs, ACTs, and IRS, as described above. All per-capita variables were continuous measures of aid in constant 2014 US dollars, as described above. $Population\_size_{jt}$ was a time-varying continuous measure of population size in country *j* in year *t*. $\alpha_j$ was a full set of country dummies to control for baseline country characteristics and $\gamma_t$ was a full set of year dummies to account for secular trends.

The coefficient of interest in Model (8) was $\mu$, which represented the average annual percentage change in ITNs, ACTs and IRS coverage as a function of an additional per-capita PMI aid spent annually. Robust standard errors were calculated to correct for potential heteroskedasticity of the error term.

***Association between PMI and study outcomes over time***

We examined whether the association between PMI and all-cause under-5 mortality trends differed over time by fitting Model (9):

$$(9)\ Y_{ijt} = \alpha_j + \chi\, PMIyear_{jt} + \delta\, GFyear_{jt} + \phi\, PEPFARyear_{jt} + \lambda\, Z_{ijt} + \gamma_t + \varepsilon_{ijt}$$

where $Y_{ijt}$ was the outcome variable set to 1 if a child *i* from country *j* in year *t* died and 0 otherwise. In these models, *POST*PMI* interaction term in Models (1-3) was substituted with a vector of binary variables indicating year of program implementation (e.g. $PMIyear1_{jt}$ set equal to 1 if PMI was in first year of implementation or 0 otherwise, $PMIyear2_{jt}$ set equal to 1 if PMI was in second year of program implementation or 0 otherwise, etc.). $GFyear_{jt}$ was a vector of binary indicators for year of Global Fund and $PEPFARyear_{jt}$ was a vector of binary indicators for year of PEPFAR program implementation. The coefficients of interest in Model (9) were a vector of $\chi$ *coefficients* which measured the annual relative risk change in child mortality as a function of PMI over time.

Lastly, we examined whether the association between PMI and population coverage of malaria intervention different over time by fitting Model (10):

$$(10)\ Y_{jt} = \alpha_j + \sigma\, PMIyear_{jt} + \delta\, GFyear_{jt} + \phi\, PEPFARyear_{jt} + \pi\, population\_size_{jt} + \gamma_t + \varepsilon_{ijt}$$

where $Y_{jt}$ were country-level continuous outcome variables of population coverage of ITNs, ACTs, and IRS, as described above. $PMIyear_{jt}$ was a vector of binary variables indicating year of PMI program implementation (e.g. $PMIyear1_{jt}$ set equal to 1 if PMI was in first year of implementation or 0 otherwise, $PMIyear2_{jt}$ set equal to 1 if PMI was in second year of program implementation or 0 otherwise, etc.). The model also included a vector of binary indicators for year of Global Fund and PEPFAR program implementation. The coefficients of interest in Model (10) were a vector of $\sigma$ *coefficients* which measured the annual percentage change in ITN, ACT and IRs coverage as a function of PMI over time.

***Parallel trends assumption test and sensitivity analysis***

The difference-in-differences design relies on the assumption that, in the absence of any intervention, countries receiving PMI funding would have identical *trends* in outcomes as non-recipient countries. We tested this "parallel trends" assumption by fitting the model shown in Model (11):

$$(11)\ Y_{ijt} = \alpha_j + \beta\, PMI_j + \delta\, Year_t + \gamma\, PMI_j * Year_t + \lambda\, Z_{ijt} + \varepsilon_{ijt}$$

where $Y_{ijt}$ was the outcome variable set to 1 if a child *i* from country *j* in year *t* died and 0 otherwise. $PMI_j$ variable was set to 1 if child *i* resided in country *j* that was eventually selected to receive PMI funds. $Year_t$ was a linear time trend, in years. The coefficient of interest was $\gamma$, which shows whether the trends in countries that were eventually selected to receive PMI had different trends before the implementation of this intervention than the comparison countries. The coefficient $\delta$ showed the overall time trends in the SSA region before PMI was implemented and $\beta$ compared baseline mortality between PMI and comparison countries. $Z_{ijt}$ *was* a vector of descriptive characteristics: child's age (binary indicators for each year of child's life), child's gender (binary indicator for female), mother's age (continuous measure of age), mother's education (binary indicators for no education, primary education, and secondary of higher education), mother's parity (continuous measure of the number of births given by the mother),

urban/rural setting (binary indicator for rural), wealth index (binary indicators for wealth quintile of the household). $\alpha_j$ *was* a full set of country dummies to control for differences between countries.

We performed several sensitivity analyses to verify our results. First, we excluded deaths that occurred in the first month of the child's life to make sure that neonatal mortality was not driving our study results. Reductions in neonatal mortality can be attributed to better prenatal and delivery care rather than the malaria interventions that we wish to identify with our PMI models. Second, we tested whether results varied by area of residence. We hypothesized that the association between PMI and child mortality in rural areas would be stronger than in urban areas because malaria burden is much higher in rural areas. Third, we separately excluded each individual country from the analysis to ensure that no single country was driving the results. Fourth, we excluded Democratic Republic of Congo and Nigeria because PMI programs were implemented at sub-national scale in these two countries and under-5 mortality from malaria was especially high there [14]. We tested whether the results were robust to the type of model we ran by estimating logit, probit, and Cox models. We also confirmed that the parallel trends assumption held when we interacted a nonlinear time trend with PMI program indicators using data from pre-PMI years. Lastly, we confirmed that we were able to detect the association between PMI and malaria intervention coverage using alternative data sources

## Appendix 1 Table B. Descriptive characteristics of sample by PMI recipient and control countries

| Indicator | PMI countries | Comparison countries |
|---|---|---|
| Number of child-year observations | 5,837,998 | 1,914,073 |
| Number of children in sample | 1,586,824 | 526,127 |
| Number of child deaths in sample | 148,551 | 50,930 |
| Female, % | 49.52 | 49.61 |
| Age < 1 year, % | 23.29 | 23.30 |
| Age < 2 years, % | 21.59 | 21.64 |
| Age < 3 years, % | 19.61 | 19.59 |
| Age < 4 years, % | 18.37 | 18.34 |
| Age < 5 years, % | 17.13 | 17.13 |
| Age at death, mean | 2.50 | 2.69 |
| Mother no education, % | 47.15 | 56.89 |
| Mother primary education, % | 36.89 | 23.54 |
| Mother secondary education, % | 14.10 | 18.23 |
| Mother higher education, % | 1.86 | 1.33 |
| Missing mother's education, % | <1 | <1 |
| Mother's age, mean | 27.77 | 27.73 |
| Parity, mean | 3.50 | 3.45 |
| Wealth index, mean | 2.73 | 2.68 |
| Missing wealth index, mean % | 3.5 | 4.8 |
| Female household head, % | 20.35 | 19.81 |
| Rural, % | 73.30 | 68.67 |

**Abbreviations:** %, Percent; PMI, President's Malaria Initiative

**Notes:** Sample based on Demographic and Health Surveys from 32 sub-Saharan countries from 1995-2014. PMI recipient countries: Angola, Benin, Congo DRC, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Tanzania, Uganda, Zambia. Comparison countries: Burkina Faso, Burundi, Cameroon, Chad, Congo, Cote d'Ivoire, Gabon, Namibia, Niger, Sierra Leone, Swaziland, The Gambia, and Togo. We report percentage of missing observations for the variables that have any missing data.

**Appendix 1 Table C. Baseline under-5 mortality rate, PfPR transmission in 2-10 year olds, ITN coverage, ACT coverage, and IRS coverage in study countries.**

| | Under-5 mortality rate (per 1,000 live births) in 2005 | Population weighted $Pf Pr_{2-10}$ in 2005 | ITN coverage in 2005 | ACT coverage in 2005 | IRS coverage in 2005 |
|---|---|---|---|---|---|
| PMI countries | 121 | 30.0 | 10.3 | 1.5 | 2.9 |
| Angola | 204 | 27.9 | 4.9 | 0.7 | 3.6 |
| Benin | 126 | 41.1 | 7.9 | 0.3 | 0 |
| Congo, DRC | 138 | 61.7 | 6.0 | 0.4 | 0 |
| Ethiopia | 109 | 3.4 | 0 | 2.3 | 7.7 |
| Ghana | 87 | 41.7 | 10.9 | 1.6 | 0 |
| Guinea | 137 | 44.4 | 0.0 | 0.7 | 0 |
| Kenya | 86 | 10.9 | 19.2 | 0.4 | 1.7 |
| Liberia | 125 | 46.4 | 21.4 | 1.0 | 0 |
| Madagascar | 81 | 18.9 | 10.4 | 0.5 | 2.2 |
| Malawi | 116 | 26.1 | 26.4 | 2.7 | 0 |
| Mali | 172 | 49.6 | 0.0 | 4.1 | 0 |
| Mozambique | 134 | 42.3 | 4.9 | 0.9 | 0 |
| Nigeria | 158 | 43.1 | 0 | 0.5 | 0 |
| Rwanda | 111 | 4.7 | 14.3 | 1.8 | 0 |
| Senegal | 96 | 9.4 | 9.6 | 2.5 | 0 |
| Tanzania | 92 | 56.5 | 31.6 | 0.7 | 0 |
| Uganda | 107 | 20.5 | 16.2 | 3.6 | 0 |
| Zambia | 112 | 19.3 | 11.4 | 4.6 | 10.9 |
| Zimbabwe | 102 | 2.5 | 0.9 | 0.2 | 29.8 |
| Comparison countries | 128 | 30.2 | 3.5 | 1.6 | 2.3 |
| Burkina Faso | 158 | 55.4 | 0 | 0.1 | 0 |
| Burundi | 127 | 23.9 | 9.0 | 3.1 | 7.9 |
| Cameroon | 125 | 47.0 | 0 | 3.4 | 0 |
| Chad | 177 | 15.4 | 0 | 0.4 | 0 |
| Congo | 95 | 34.0 | 0 | 5.3 | 0 |
| Côte d'Ivoire | 129 | 67.9 | 0 | 0.6 | 0 |
| Gabon | 77 | 12.5 | 15.8 | 2.1 | 0 |
| Namibia | 98 | 8.8 | 0 | 1.2 | 21.9 |
| Niger | 72 | 26.7 | 0 | 1.9 | 0 |
| Sierra Leone | 173 | 49.7 | 0 | 1.2 | 0 |
| Swaziland | 204 | <1 | 0 | 0.2 | 0 |
| The Gambia | 130 | 6.7 | 20.6 | 0.1 | 0 |
| Togo | 105 | 44.5 | 0 | 1.1 | 0 |

**Data sources:** World Development Indicators and Malaria Atlas Project.

**Abbreviations**: ITNs=estimated proportion of people who slept under an insecticide-treated bednet on any given night; ACTs=estimated proportion of cases of fever in under-5 year olds that were treated with Artemisinin Combination Therapy; IRS=estimated proportion of the population protected by indoor residual spraying of insecticides.

**Notes:** Under-5 mortality rate represents the probability per 1,000 that a newborn baby will die before reaching age five, if subject to age-specific mortality rates of the specified year. The numbers presented in row labeled "PMI countries" represent the mean values for PMI countries. The numbers presented on row labeled "Comparison countries" represent the mean values for comparison countries.

**Main Study Results Displaying Individual-Level and Household-Level Covariates**

**Appendix 1 Table D. Modified Poisson regression models of child mortality and implementation of large-scale healthcare interventions in sub-Saharan Africa from 1995 to 2014**

| | Relative risk of under-5 mortality (1) | Relative risk of under-5 mortality (2) | Relative risk of under-5 mortality (3) |
|---|---|---|---|
| | RR [95%CI] | RR [95%CI] | RR [95%CI] |
| *Implemented program* | | | |
| Post PMI | 0.85** [0.74 - 0.96] | 0.84** [0.74 - 0.95] | 0.84** [0.74 - 0.96] |
| Post Global Fund | | 0.95 [0.87 - 1.04] | 0.93 [0.85 - 1.02] |
| Post PEPFAR | | 1.06 [0.96 - 1.17] | 1.05 [0.95 - 1.17] |
| *Child's characteristics* | | | |
| Female | | | 0.88*** [0.87 - 0.89] |
| Age (<1 year) | | | Ref. |
| Age < 2 years | | | 1.59*** [1.46 - 1.74] |
| Age < 3 years | | | 0.57*** [0.49 - 0.65] |
| Age < 4 years | | | 0.39*** [0.35 - 0.43] |
| Age < 5 years | | | 0.24*** [0.21 - 0.26] |
| *Mother's characteristics* | | | |
| No education | | | Ref. |
| Primary education | | | 0.90*** [0.86 - 0.94] |
| Secondary education | | | 0.79*** [0.75 - 0.82] |
| Higher education | | | 0.71*** [0.65 - 0.78] |
| Age | | | 0.94*** [0.93 - 0.94] |
| Parity | | | 1.18*** [1.17 - 1.19] |
| *Household characteristics* | | | |
| Lowest wealth quintile | | | Ref. |
| Second wealth quintile | | | 0.99 [0.94 - 1.04] |
| Middle wealth quintile | | | 0.95* [0.91 - 1.00] |
| Fourth wealth quintile | | | 0.88*** [0.82 - 0.95] |
| Highest wealth quintile | | | 0.72*** [0.68 - 0.76] |
| Female household head | | | 1.02 [0.99 - 1.04] |
| Rural residence | | | 1.09*** [1.04 - 1.13] |
| No. observations | 7,752,071 | 7,752,071 | 7,404,578 |
| Country FE | Yes | Yes | Yes |
| Year FE | Yes | Yes | Yes |

**Data Source:** Demographic Health Surveys.

**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.

**Notes:** Numbers 1, 2 and 3 refer to the Model number, specified in Statistical Analysis section. All models also included country fixed effects to control for baseline characteristics of countries and year fixed effects to control for secular trends. Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

## Appendix 1 Table E. Modified Poisson regression models of child mortality and development assistance for health in sub-Saharan Africa from 1995 to 2012

| | Annual risk of under-5 mortality (4) | Relative risk of under-5 mortality (5) | Relative risk of under-5 mortality (6) |
|---|---|---|---|
| | RR [95%CI] | RR [95%CI] | RR [95%CI] |
| *Per-capita aid disbursements (US$)* | | | |
| PMI (US bilateral aid for malaria) | 0.84*** [0.77 - 0.90] | 0.85*** [0.78 - 0.92] | 0.86*** [0.79 - 0.93] |
| Global Fund (malaria only) | | 0.96* [0.93 - 1.00] | 0.96 [0.93 - 1.00] |
| Other aid for malaria | | 1.04 [0.89 - 1.21] | 1.04 [0.87 - 1.24] |
| Global Fund (HIV/AIDS and TB) | | 1.00 [0.96 - 1.03] | 1.00 [0.96 - 1.03] |
| PEPFAR (US bilateral aid for HIV/AIDS) | | 1.01 [0.99 - 1.02] | 1.01 [0.99 - 1.02] |
| All other disbursements for health | | 0.99 [0.98 - 1.01] | 1.00 [0.98 - 1.01] |
| *Child's characteristics* | | | |
| Female | | | 0.88*** [0.87 - 0.89] |
| Age (<1 year) | | | *Ref.* |
| Age < 2 years | | | 1.59*** [1.45 - 1.73] |
| Age < 3 years | | | 0.57*** [0.49 - 0.65] |
| Age < 4 years | | | 0.39*** [0.35 - 0.42] |
| Age < 5 years | | | 0.23*** [0.21 - 0.26] |
| *Mother's characteristics* | | | |
| No education | | | *Ref.* |
| Primary education | | | 0.90*** [0.87 - 0.94] |
| Secondary education | | | 0.79*** [0.76 - 0.82] |
| Higher education | | | 0.72*** [0.67 - 0.78] |
| Age | | | 0.94*** [0.93 - 0.94] |
| Parity | | | 1.18*** [1.17 - 1.19] |
| *Household characteristics* | | | |
| Lowest wealth quintile | | | *Ref.* |
| Second wealth quintile | | | 0.98 [0.94 - 1.03] |
| Middle wealth quintile | | | 0.95 [0.91 - 1.00] |
| Fourth wealth quintile | | | 0.88*** [0.82 - 0.95] |
| Highest wealth quintile | | | 0.73*** [0.69 - 0.77] |
| Female household head | | | 1.02 [0.99 - 1.05] |
| Rural residence | | | 1.09*** [1.04 - 1.14] |
| No. observations | 7,140,735 | 7,140,735 | 6,829,406 |
| Country FE | Yes | Yes | Yes |
| Year FE | Yes | Yes | Yes |

**Data Sources:** Demographic Health Surveys, Development Assistance for Health Database, and World Development Indicators.
**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.
**Notes:** Numbers 4, 5 and 6 refer to the Model number specified in Statistical Analysis section. All models also included country fixed effects to control for baseline characteristics of countries and year fixed effects to control for secular trends. Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

## Plausibility of Study Findings

We used estimates from prior studies to calculate the plausible reductions in all-cause child mortality that would result from the PMI-associated increases in ITN, ACT, and IRS coverage that we reported in Table 5. These prior studies were conducted in two specific settings in sub-Saharan Africa. We used evidence from Kenya, where Fegan et al. (2007) estimated that increasing ITN coverage from 7% to 67% was associated with 44% reduction in all-cause child mortality [15]. We chose to rely on this study rather than results from efficacy trials [16] because the procedures of this study more closely resembled large-scale campaigns of ITN distribution that are supported with PMI funds than controlled experiments. Given the limited evidence about the impact of IRS on child mortality [17], we followed the example of Eisele et al. (2010) and assumed that IRS coverage had approximately equal protective effect to ITNs [18]. Finally, we used evidence from Zanzibar, where Bhattarai et al. (2007) found that reaching high coverage of ACTs (we used the conservative assumption that this implied full coverage) was associated 52% reduction in child mortality [19]. Applying these effect sizes of increased malaria intervention coverage on all-cause mortality to the PMI-associated increases in intervention coverage we obtained in our study (8.34 percentage point increase in ITN coverage, 6.63 percentage point increase in IRS coverage, and 2.98 percentage point increase in ACT coverage), we predicted the following reductions in all-cause child mortality: 6.12% from ITNs, 4.86% from IRS, and 1.55 from ACTs. The increased coverage of these three prevention and treatment modalities could therefore plausibly account for a 12.5% reduction in all-cause child mortality. These calculations should be interpreted with caution given the assumptions stated above, the reliance on estimates from two country settings to 32 different countries in SSA, and the fact that the increases in coverage detected in our study were considerably smaller in magnitude than those that were assumed or estimated in the other studies. Our calculations also did not account for interactive effects between ITNs, IRS and ACTs.

## Additional Models of Population Coverage of Malaria Interventions and PMI Program Implementation

### Appendix 1 Table F. Population coverage of insecticide treated nets (ITNs), artemisinin-based combination therapy (ACTs), and indoor residual spraying (IRS) in 19 PMI-recipient countries compared to 22 non-recipient countries in sub-Saharan Africa

| Panel A (2000-2014) | Models of population coverage of malaria interventions and program implementation **in 19 PMI-recipient countries compared to 22 non-recipient countries** | | |
|---|---|---|---|
| | ITN coverage | ACT coverage | IRS coverage |
| | Coef. [95% CI] | Coef. [95% CI] | Coef. [95% CI] |
| *Implemented program* | | | |
| Post PMI | 10.11** [3.49 - 16.73] | 5.64* [0.03 - 11.25] | 7.69** [2.42 - 12.96] |
| Post Global Fund | -4.74 [-12.25 - 2.77] | 1.34 [-3.37 - 6.05] | 1.37 [-2.79 - 5.54] |
| Post PEPFAR | -4.09 [-10.20 - 2.01] | 0.26 [-3.13 - 3.65] | -0.54 [-3.67 - 2.59] |
| No. observations (country-years) | 655 | 655 | 655 |

| Panel B (2000-2014) | Models of population coverage of malaria interventions and per-capita disbursements for health **in 19 PMI-recipient countries compared to 22 non-recipient countries** | | |
|---|---|---|---|
| | ITN coverage | ACT coverage | IRS coverage |
| | Coef. [95% CI] | Coef. [95% CI] | Coef. [95% CI] |
| *Per capita aid disbursement (US$)* | | | |
| US bilateral aid for malaria | 4.29* [0.54, 8.03] | 3.56 [-0.07, 7.19] | 1.98 [-1.32, 5.27] |
| Other aid for malaria | 9.69** [3.41, 15.97] | 1.70 [-4.40, 7.80] | 1.90 [-8.15, 11.95] |
| Global Fund (malaria only) | 1.51 [-0.02, 3.05] | 0.27 [-0.81, 1.35] | 0.11 [-1.33, 1.54] |
| Global Fund (HIV/AIDS and TB) | -0.22 [-0.77, 0.34] | -0.12 [-0.38, 0.15] | 0.61* [0.15, 1.08] |
| US bilateral aid for HIV/AIDS | -0.39* [-0.73, -0.04] | -0.03 [-0.26, 0.20] | -0.15 [-0.75, 0.45] |
| All other disbursements for health | -0.39 [-1.18, 0.39] | -0.15 [-0.74, 0.44] | 0.16 [-0.48, 0.79] |
| No. observations (country-years) | 527 | 527 | 527 |

**Data sources:** Malaria Atlas Project, Development Assistance for Health Database, and World Development Indicators.
**Abbreviations**: Coef.=coefficient; 95% CI=95% confidence interval; ITNs=estimated proportion of people who slept under an insecticide-treated bednet on any given night; ACTs=estimated proportion of cases of fever in under-5 year olds that were treated with Artemisinin Combination Therapy; IRS=estimated proportion of the population protected by indoor residual spraying of insecticides.
**Notes:** Coefficients can be interpreted as percent changes. Countries in the sample include all 19 PMI-recipient countries (Angola, Benin, Democratic Republic of Congo, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Malawi, Mali, Mozambique, Nigeria, Rwanda, Senegal, Tanzania, Uganda, Zambia, and Zimbabwe) and 22 PMI non-recipient countries (Botswana, Burkina Faso, Burundi, Cameroon, Chad, Central African Republic, Congo, Cote d'Ivoire, Equatorial Guinea, Eritrea, Gabon, The Gambia, Guinea-Bissau, Mauritania, Namibia, Niger, Sierra Leone, Somalia, South Sudan, Sudan, Swaziland, and Togo). Data from South Africa were also available but these were excluded because the country was an outlier (results with SA available from authors). All models also included country and year fixed effects and population size. Robust standard errors were used to calculate confidence intervals and p-values. P-value notation: *** p<0.001, ** p<0.01, * p<0.05.

**Appendix 1 Table G. Association between child mortality/malaria intervention coverage and year of PMI program implementation**

| Annual risk of child mortality and year of PMI program implementation (9) | | Population coverage of malaria interventions and year of PMI program implementation (10) | | | |
|---|---|---|---|---|---|
| | Child mortality RR [95%CI] | | ITNs Coef [95%CI] | ACTs Coef [95%CI] | IRS Coef [95%CI] |
| *Year of PMI program* | | *Year of PMI program* | | | |
| Year 1 | 0.93 [0.86 - 1.01] | Year 1 | 4.61 [-0.24 - 9.47] | 1.36 [-1.83 - 4.55] | 7.07* [1.31 - 12.83] |
| Year 2 | 0.82** [0.71 - 0.94] | Year 2 | 2.97 [-2.39 - 8.33] | 2.87 [-0.24 - 5.98] | 6.88** [1.97 - 11.79] |
| Year 3 | 0.77*** [0.66 - 0.89] | Year 3 | 6.17* [1.10 - 11.23] | 4.53 [-0.44 - 9.50] | 8.29** [2.84 - 13.74] |
| Year 4 | 0.73*** [0.61 - 0.88] | Year 4 | 7.85** [2.02 - 13.69] | 5.98* [1.44 - 10.52] | 9.97*** [4.43 - 15.50] |
| Year 5 | 0.65** [0.48 - 0.88] | Year 5 | 9.50** [2.82 - 16.19] | 5.26* [0.24 - 10.28] | 4.43 [-1.38 - 10.24] |
| Year 6 | 0.59* [0.37 - 0.94] | Year 6 | 12.51* [2.89 - 22.13] | 2.38 [-3.82 - 8.57] | 3.64 [-1.86 - 9.15] |
| Year 7 | 0.43 [0.15 - 1.25] | Year 7 | 16.52*** [7.45 - 25.60] | 5.68 [-0.65 - 12.00] | 5.81* [0.65 - 10.96] |
| Year 8 | 0.68 [0.17 - 2.71] | Year 8 | 17.37** [5.59 - 29.15] | 5.37 [-2.71 - 13.45] | 3.50 [-1.96 - 8.97] |
| Year 9 | Data not available | Year 9 | 6.04 [-17.94 - 30.02] | 16.16* [0.73 - 31.58] | -2.09 [-9.75 - 5.57] |
| No. observations (child-years) | 7,404,578 | No. observations (country-years) | 480 | 480 | 480 |
| GF year FE | Yes | GF year FE | Yes | Yes | Yes |
| PEPFAR year FE | Yes | PEPFAR year FE | Yes | Yes | Yes |
| Country FE | Yes | Country FE | Yes | Yes | Yes |
| Year FE | Yes | Year FE | Yes | Yes | Yes |
| Individual covariates | Yes | Population size | Yes | Yes | Yes |

**Data Source:** Demographic Health Surveys, Development Assistance for Health Database.
**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.
**Notes:** All models also included country fixed effects to control for baseline characteristics of countries and year fixed effects to control for secular trends. Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

## Robustness Checks

### Appendix 1 Table H. Sensitivity analysis excluding neonatal deaths from the model (i.e. deaths before reaching one month of age)

| Models of child mortality and program implementation | RR [95%CI] | Models of child mortality and per-capita disbursements for health | RR [95%CI] |
|---|---|---|---|
| *Implemented program* | | *Per-capita aid disbursements (US$)* | |
| Post PMI | 0.79*** [0.69 - 0.90] | PMI (US bilateral aid for malaria) | 0.83*** [0.75 - 0.92] |
| Post Global Fund | 0.95 [0.86 - 1.04] | Global Fund (malaria only) | 0.96 [0.93 - 1.00] |
| Post PEPFAR | 1.03 [0.92 - 1.16] | Other aid for malaria | 1.03 [0.84 - 1.26] |
| | | Global Fund (HIV/AIDS and TB) | 1.00 [0.96 - 1.03] |
| | | PEPFAR (US bilateral aid for HIV/AIDS) | 1.00 [0.99 - 1.02] |
| | | All other disbursements for health | 1.00 [0.98 - 1.01] |
| *Child's characteristics* | | *Child's characteristics* | |
| Female | 0.94*** [0.93 - 0.96] | Female | 0.94*** [0.92 - 0.96] |
| Age in years | 0.94*** [0.92 - 0.96] | Age in years | 0.94*** [0.92 - 0.96] |
| *Mother's characteristics* | | *Mother's characteristics* | |
| No education | Ref. | No education | Ref. |
| Primary education | 0.86*** [0.81 - 0.92] | Primary education | 0.87*** [0.82 - 0.92] |
| Secondary education | 0.71*** [0.67 - 0.75] | Secondary education | 0.71*** [0.67 - 0.76] |
| Higher education | 0.53*** [0.48 - 0.59] | Higher education | 0.54*** [0.49 - 0.59] |
| Age | 0.94*** [0.93 - 0.94] | Age | 0.94*** [0.93 - 0.94] |
| Parity | 1.19*** [1.17 - 1.20] | Parity | 1.19*** [1.17 - 1.20] |
| *Household characteristics* | | *Household characteristics* | |
| Lowest wealth quintile | Ref. | Lowest wealth quintile | Ref. |
| Second wealth quintile | 0.98 [0.93 - 1.04] | Second wealth quintile | 0.98 [0.92 - 1.04] |
| Middle wealth quintile | 0.94* [0.89 - 1.00] | Middle wealth quintile | 0.94 [0.89 - 1.00] |
| Fourth wealth quintile | 0.86** [0.78 - 0.94] | Fourth wealth quintile | 0.86** [0.78 - 0.95] |
| Highest wealth quintile | 0.64*** [0.59 - 0.70] | Highest wealth quintile | 0.65*** [0.59 - 0.71] |
| Female household head | 1.02 [0.99 - 1.05] | Female household head | 1.02 [0.99 - 1.05] |
| Rural residence | 1.12*** [1.07 - 1.17] | Rural residence | 1.12*** [1.07 - 1.17] |
| No. observations | 7,344,822 | No. observations | 6,920,625 |
| Country FE | Yes | Country FE | Yes |
| Year FE | Yes | Year FE | Yes |

**Data Source:** Demographic Health Surveys, Development Assistance for Health Database.
**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.
**Notes:** All models also included country fixed effects to control for baseline characteristics of countries and year fixed effects to control for secular trends. Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

## Appendix 1 Table I. Child mortality trends after PMI program implementation stratified by urban/rural residence

| Association between PMI and under-5 mortality by rural/urban area of residence | | |
|---|---|---|
| | Rural | Urban |
| | RR [95% CI] | RR [95% CI] |
| *Implemented program* | | |
| Post PMI | 0.83** [0.73 - 0.95] | 0.87* [0.76 - 1.00] |
| Post Global Fund | 0.94 [0.84 - 1.06] | 0.93* [0.87 – 0.99] |
| Post PEPFAR | 1.03 [0.92 - 1.16] | 1.12 [0.99 - 1.27] |
| *Child's characteristics* | | |
| Female | 0.89*** [0.88 - 0.90] | 0.85*** [0.83 - 0.87] |
| Age (<1 year) | *Ref.* | *Ref.* |
| Age < 2 years | 1.68*** [1.54 - 1.83] | 1.33*** [1.21 - 1.47] |
| Age < 3 years | 0.62*** [0.53 - 0.71] | 0.41*** [0.37 - 0.46] |
| Age < 4 years | 0.43*** [0.39 - 0.47] | 0.29*** [0.26 - 0.32] |
| Age < 5 years | 0.25*** [0.23 - 0.27] | 0.19*** [0.17 - 0.22] |
| *Mother's characteristics* | | |
| No education | *Ref.* | *Ref.* |
| Primary education | 0.90*** [0.86 - 0.94] | 0.91*** [0.86 - 0.95] |
| Secondary education | 0.79*** [0.75 - 0.84] | 0.77*** [0.73 - 0.82] |
| Higher education | 0.73*** [0.64 - 0.83] | 0.69*** [0.63 - 0.75] |
| Age | 0.94*** [0.93 - 0.94] | 0.94*** [0.94 - 0.95] |
| Parity | 1.18*** [1.17 - 1.19] | 1.18*** [1.16 - 1.20] |
| *Household characteristics* | | |
| Lowest wealth quintile | *Ref.* | *Ref.* |
| Second wealth quintile | 0.99 [0.93 - 1.04] | 1.00 [0.94 - 1.06] |
| Middle wealth quintile | 0.96 [0.92 - 1.00] | 0.90** [0.85 - 0.97] |
| Fourth wealth quintile | 0.90** [0.83 - 0.96] | 0.82*** [0.75 - 0.90] |
| Highest wealth quintile | 0.74*** [0.69 - 0.79] | 0.69*** [0.64 - 0.76] |
| Female household head | 1.01 [0.98 - 1.04] | 1.05** [1.02 - 1.09] |
| Rural residence | - | - |
| No. observations | 5,348,156 | 2,056,422 |
| Country FE | Yes | Yes |
| Year FE | Yes | Yes |

| Association between aid disbursements and under-5 mortality by rural/urban area of residence | | |
|---|---|---|
| | Rural | Urban |
| | RR [95% CI] | RR [95% CI] |
| *Per-capita aid disbursements (US$)* | | |
| PMI (US bilateral aid for malaria) | 0.85*** [0.78 - 0.93] | 0.88*** [0.82 - 0.93] |
| Global Fund (malaria only) | 0.96* [0.92 - 0.99] | 0.98 [0.94 - 1.03] |
| Other aid for malaria | 1.01 [0.83 - 1.21] | 1.11 [0.97 - 1.28] |
| Global Fund (HIV/AIDS and TB) | 0.99 [0.96 - 1.03] | 1.01 [0.99 - 1.03] |
| PEPFAR (US bilateral aid for HIV/AIDS) | 1.00 [0.99 - 1.02] | 1.01 [1.00 - 1.01] |
| All other disbursements for health | 0.99 [0.98 - 1.01] | 1.00 [0.98 - 1.01] |
| *Child's characteristics* | | |
| Female | 0.89*** [0.88 - 0.90] | 0.84*** [0.82 - 0.86] |
| Age (<1 year) | *Ref.* | *Ref.* |
| Age < 2 years | 1.67*** [1.53 - 1.83] | 1.33*** [1.20 - 1.47] |
| Age < 3 years | 0.62*** [0.53 - 0.71] | 0.41*** [0.36 - 0.46] |
| Age < 4 years | 0.42*** [0.38 - 0.46] | 0.28*** [0.25 - 0.32] |
| Age < 5 years | 0.25*** [0.23 - 0.27] | 0.18*** [0.16 - 0.20] |
| *Mother's characteristics* | | |
| No education | *Ref.* | *Ref.* |
| Primary education | 0.91*** [0.86 - 0.95] | 0.91*** [0.87 - 0.96] |
| Secondary education | 0.79*** [0.75 - 0.84] | 0.78*** [0.73 - 0.82] |
| Higher education | 0.74*** [0.67 - 0.81] | 0.70*** [0.64 - 0.76] |
| Age | 0.94*** [0.93 - 0.94] | 0.94*** [0.94 - 0.95] |
| Parity | 1.18*** [1.17 - 1.19] | 1.18*** [1.16 - 1.20] |
| *Household characteristics* | | |
| Lowest wealth quintile | *Ref.* | *Ref.* |
| Second wealth quintile | 0.98 [0.93 - 1.04] | 1.00 [0.94 - 1.06] |
| Middle wealth quintile | 0.96 [0.91 - 1.01] | 0.91** [0.85 - 0.97] |
| Fourth wealth quintile | 0.90** [0.84 - 0.97] | 0.82*** [0.75 - 0.90] |
| Highest wealth quintile | 0.75*** [0.70 - 0.79] | 0.70*** [0.64 - 0.76] |
| Female household head | 1.01 [0.98 - 1.04] | 1.06** [1.02 - 1.09] |
| Rural residence | - | - |
| No. observations | 4,939,048 | 1,890,358 |
| Country FE | Yes | Yes |
| Year FE | Yes | Yes |

**Data Source:** Demographic Health Surveys, Development Assistance for Health Database.
**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.
**Notes:** All models also included country fixed effects to control for baseline characteristics of countries and year fixed effects to control for secular trends. Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

**Appendix 1 Table J. Sensitivity analysis excluding individual countries from the model**

| Models excluding PMI countries | |
|---|---|
| Excluded country | RR [95%CI] |
| Angola | 0.83** [0.73 - 0.95] |
| Benin | 0.83** [0.73 - 0.95] |
| Congo, DRC | 0.82** [0.72 - 0.94] |
| Ethiopia | 0.84** [0.73 - 0.96] |
| Ghana | 0.83** [0.73 - 0.95] |
| Guinea | 0.84** [0.73 - 0.96] |
| Kenya | 0.83** [0.72 - 0.95] |
| Liberia | 0.85* [0.74 - 0.97] |
| Madagascar | 0.86* [0.76 - 0.97] |
| Malawi | 0.84* [0.73 - 0.97] |
| Mali | 0.84** [0.73 - 0.96] |
| Mozambique | 0.83** [0.73 - 0.95] |
| Nigeria | 0.84* [0.73 - 0.98] |
| Rwanda | 0.85* [0.75 - 0.97] |
| Senegal | 0.84* [0.72 - 0.97] |
| Tanzania | 0.86* [0.76 - 0.98] |
| Uganda | 0.83** [0.72 - 0.95] |
| Zambia | 0.83** [0.73 - 0.95] |
| Zimbabwe | 0.84** [0.74 - 0.96] |

| Models excluding control countries | |
|---|---|
| Excluded country | RR [95%CI] |
| Burkina Faso | 0.82** [0.72 - 0.93] |
| Burundi | 0.82** [0.72 - 0.93] |
| Cameroon | 0.84** [0.73 - 0.96] |
| Chad | 0.84** [0.74 - 0.96] |
| Congo | 0.83** [0.73 - 0.95] |
| Cote d'Ivoire | 0.84** [0.74 - 0.96] |
| Gabon | 0.84** [0.74 - 0.95] |
| Namibia | 0.85* [0.74 - 0.96] |
| Niger | 0.83** [0.72 - 0.95] |
| Sierra Leone | 0.86* [0.76 - 0.98] |
| Swaziland | 0.84** [0.74 - 0.96] |
| The Gambia | 0.84** [0.73 - 0.95] |
| Togo | 0.85* [0.75 - 0.97] |

| Models excluding DRC and Nigeria | |
|---|---|
| Excluded country | RR [95%CI] |
| Nigeria and DRC | 0.82* [0.70 - 0.97] |

**Data Source:** Demographic Health Surveys.
**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative.
**Notes:** The results listed here represent average annual change in risk of all-cause under-5 mortality in PMI countries when individual counties were excluded from the analysis. All models also included interactions for PEPFAR and GF programs, country fixed effects, year fixed effects, and individual-level covariates (i.e. Model 3). Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

## Appendix 1 Table K. Under-5 mortality trends using different model specifications: Modified Poisson, Cox, Logit, and Probit

| | **Modified Poisson** (glm, SE clustered at country) | **Cox** (stcox, SE clustered at country) | **Logit** (logit, SE clustered at country) | **Probit** (probit, SE clustered at country) |
|---|---|---|---|---|
| | Coef. [95% CI] | Coef. [95% CI] | Coef. [95% CI] | Coef. [95% CI] |
| *Implemented program* | | | | |
| Post PMI | -0.18** [-0.31 - -0.05] | -0.18** [-0.31 - -0.05] | -0.18** [-0.31 - -0.04] | -0.07* [-0.12 - -0.01] |
| Post Global Fund | 0.05 [-0.06 - 0.16] | 0.05 [-0.06 - 0.16] | 0.06 [-0.06 - 0.16] | 0.02 [-0.02 - 0.07] |
| Post PEPFAR | -0.07 [-0.16 - 0.02] | -0.07 [-0.16 - 0.02] | -0.07 [-0.17 - 0.02] | -0.03 [-0.07 - 0.01] |
| *Child's characteristics* | | | | |
| Female | -0.13*** [-0.14 - -0.11] | -0.13*** [-0.14 - -0.11] | -0.13*** [-0.15 - -0.12] | -0.06*** [-0.06 - -0.05] |
| Age (<1 year) | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| Age < 2 years | 0.47*** [0.38 - 0.55] | 0.53*** [0.42 - 0.64] | 0.49*** [0.40 - 0.58] | 0.22*** [0.17 - 0.26] |
| Age < 3 years | -0.57*** [-0.71 - -0.43] | -0.43*** [-0.59 - -0.27] | -0.59*** [-0.73 - -0.45] | -0.26*** [-0.31 - -0.20] |
| Age < 4 years | -0.94*** [-1.04 - -0.84] | -0.73*** [-0.85 - -0.62] | -0.96*** [-1.06 - -0.86] | -0.40*** [-0.44 - -0.36] |
| Age < 5 years | -1.45*** [-1.55 - -1.35] | -1.24*** [-1.36 - -1.12] | -1.47*** [-1.57 - -1.38] | -0.58*** [-0.62 - -0.55] |
| *Mother's characteristics* | | | | |
| No education | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| Primary education | -0.11*** [-0.15 - -0.07] | -0.11*** [-0.15 - -0.07] | -0.11*** [-0.16 - -0.07] | -0.05*** [-0.07 - -0.03] |
| Secondary education | -0.24*** [-0.28 - -0.19] | -0.24*** [-0.28 - -0.19] | -0.25*** [-0.29 - -0.20] | -0.11*** [-0.13 - -0.08] |
| Higher education | -0.34*** [-0.43 - -0.25] | -0.34*** [-0.43 - -0.25] | -0.34*** [-0.44 - -0.25] | -0.14*** [-0.19 - -0.09] |
| Age | -0.06*** [-0.07 - -0.06] | -0.06*** [-0.07 - -0.06] | -0.07*** [-0.07 - -0.06] | -0.03*** [-0.03 - -0.03] |
| Parity | 0.16*** [0.15 - 0.18] | 0.16*** [0.15 - 0.18] | 0.17*** [0.16 - 0.18] | 0.07*** [0.07 - 0.08] |
| *Household characteristics* | | | | |
| Lowest wealth quintile | *Ref.* | *Ref.* | *Ref.* | *Ref.* |
| Second wealth quintile | -0.01 [-0.06 - 0.04] | -0.01 [-0.06 - 0.04] | -0.02 [-0.07 - 0.04] | -0.01 [-0.03 - 0.01] |
| Middle wealth quintile | -0.05* [-0.09 - -0.00] | -0.05* [-0.09 - -0.00] | -0.05* [-0.10 - -0.00] | -0.02* [-0.04 - -0.00] |
| Fourth wealth quintile | -0.13*** [-0.20 - -0.06] | -0.13*** [-0.20 - -0.06] | -0.13*** [-0.21 - -0.06] | -0.06*** [-0.09 - -0.03] |
| Highest wealth quintile | -0.33*** [-0.39 - -0.28] | -0.33*** [-0.39 - -0.28] | -0.35*** [-0.40 - -0.29] | -0.15*** [-0.17 - -0.12] |
| Female household head | 0.02 [-0.01 - 0.04] | 0.02 [-0.01 - 0.04] | 0.02 [-0.01 - 0.04] | 0.01 [-0.00 - 0.02] |
| Rural residence | 0.08*** [0.04 - 0.12] | 0.08*** [0.04 - 0.12] | 0.08*** [0.04 - 0.13] | 0.04*** [0.02 - 0.05] |
| No. observations | 7,467,239 | 7,467,239 | 7,467,239 | 7,467,239 |
| Country FE | Yes | Yes | Yes | Yes |
| Year FE | Yes | Yes | Yes | Yes |

**Data Source:** Demographic Health Surveys, Development Assistance for Health Database.
**Abbreviations:** 95% CI, 95% confidence interval; PMI, President's Malaria Initiative; PEPFAR, President's Emergency Plan for AIDS Relief.
**Notes:** All models also included country fixed effects to control for baseline characteristics of countries and year fixed effects to control for secular trends. Standard errors were clustered at the country level. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

## Appendix 1 Table L. Parallel trends assumption using non-linear time trend

| | Annual risk of child mortality prior to PMI |
|---|---|
| | RR [95% CI] |
| PMI-recipient country | 1.04 [0.96 – 1.13] |
| 1996 | 0.98 [0.92 - 1.04] |
| 1997 | 0.96 [0.86 - 1.06] |
| 1998 | 0.92 [0.81 - 1.04] |
| 1999 | 0.94 [0.82 - 1.08] |
| 2000 | 0.97 [0.87 - 1.08] |
| 2001 | 0.94 [0.82 - 1.07] |
| 2002 | 0.87* [0.78 - 0.98] |
| 2003 | 0.86* [0.74 - 0.99] |
| 2004 | 0.82** [0.73 - 0.93] |
| 2005 | 0.82* [0.70 - 0.97] |
| 2006 | 0.71** [0.57 - 0.89] |
| 2007 | 0.68*** [0.58 - 0.80] |
| 2008 | 0.63*** [0.53 - 0.75] |
| 2009 | 0.63*** [0.51 - 0.79] |
| 2010 | 0.57*** [0.45 - 0.73] |
| 2011 | 0.49*** [0.37 - 0.65] |
| 2012 | 0.37*** [0.23 - 0.58] |
| 2013 | 0.43** [0.26 - 0.72] |
| 2014 | 0.07** [0.01 - 0.40] |
| PMI-recipient country * 1996 | 0.99 [0.92 - 1.06] |
| PMI-recipient country * 1997 | 1.02 [0.91 - 1.13] |
| PMI-recipient country * 1998 | 1.05 [0.92 - 1.19] |
| PMI-recipient country * 1999 | 0.98 [0.85 - 1.13] |
| PMI-recipient country * 2000 | 0.94 [0.82 - 1.07] |
| PMI-recipient country * 2001 | 0.88 [0.75 - 1.03] |
| PMI-recipient country * 2002 | 0.90 [0.79 - 1.03] |
| PMI-recipient country * 2003 | 0.89 [0.76 - 1.05] |
| PMI-recipient country * 2004 | 0.87 [0.75 - 1.00] |
| PMI-recipient country * 2005 | 0.77* [0.63 - 0.95] |
| PMI-recipient country * 2006 | 0.87 [0.67 - 1.12] |
| PMI-recipient country * 2007 | 0.90 [0.71 - 1.13] |
| PMI-recipient country * 2008 | 0.94 [0.78 - 1.14] |
| PMI-recipient country * 2009 | 0.98 [0.76 - 1.26] |
| PMI-recipient country * 2010 | 1.06 [0.82 - 1.38] |
| No. observations (children-years) | 6,174,926 |

**Data Source:** Demographic Health Surveys.

**Abbreviations:** RR, risk ratio; 95% CI, 95% confidence interval; PMI, President's Malaria Initiative.

**Notes:** PMI-recipient country variable indicates whether a country eventually received PMI funds. Year indicators represent non-linear time trends in under-5 mortality in the study sample. The coefficients of interest are the interactions of PMI country indicator and binary indicators of year, which measure whether mortality trends in countries that eventually received PMI differed from mortality time trend in comparison countries over time, adjusted for individual-level covariates. Model also included individual-level covariates: child's age and gender, mother's level of education, age and parity, rural/urban residence, household wealth and whether the head of household is female country fixed effects. Standard errors were clustered at the country level. Sample excludes observations from PMI-recipient countries after the program was implemented. P-value notation: *** p<0.001, ** p<0.01, * p<0.05

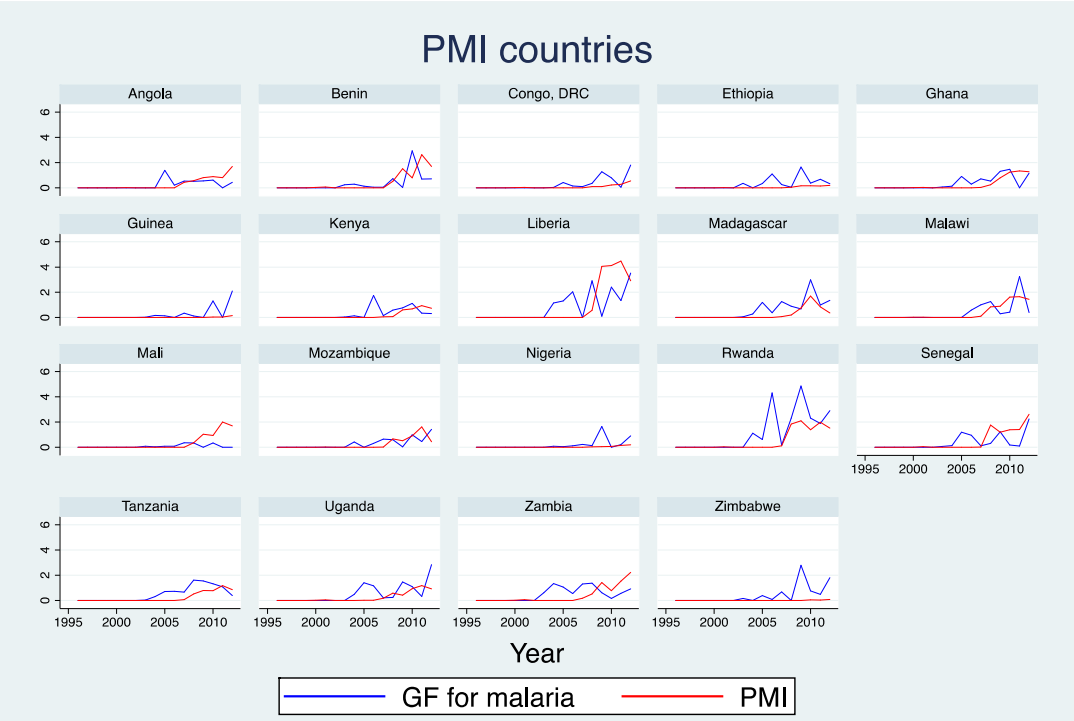
## Appendix 1 Table M. Models of malaria interventions coverage using alternative data sources

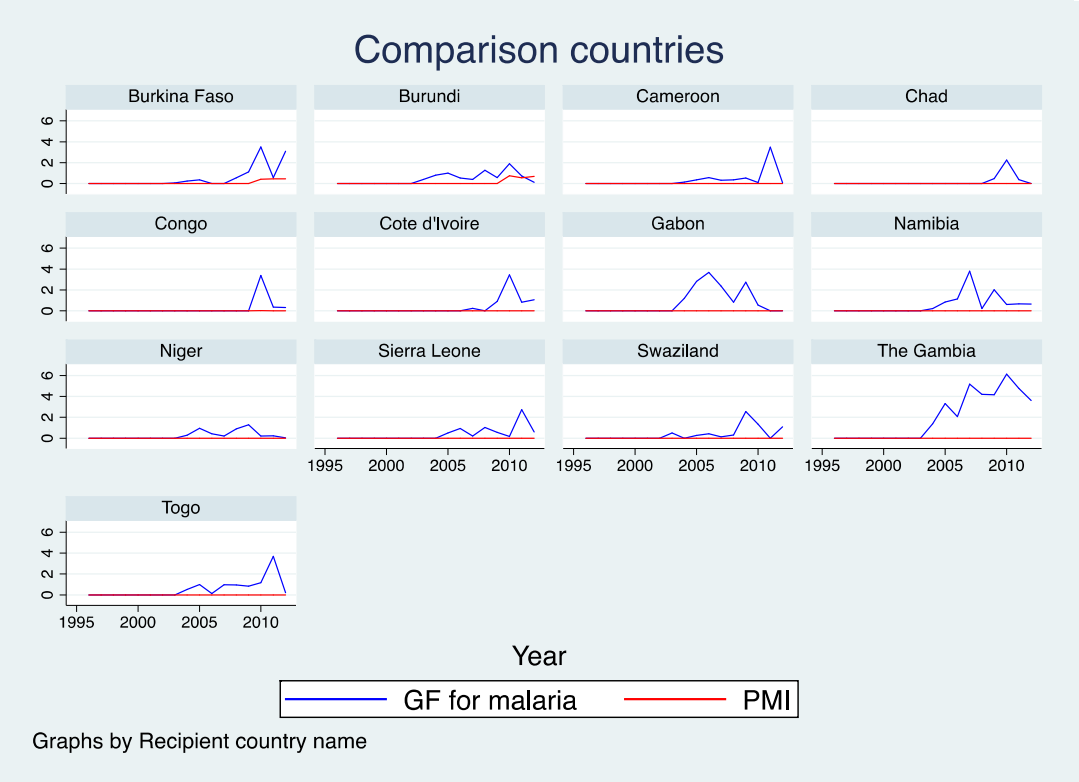
| Panel A: World DataBank (country-level) | Sensitivity analysis 1 - World Bank Data | |
|---|---|---|
| | Percentage of children under age five who slept under an ITN to prevent malaria [a] | Percentage of children under age five who were ill with fever in the last two weeks and received any appropriate anti-malarial drugs [a] |
| | Coef. [95% CI] | Coef. [95% CI] |
| *Implemented program* | | |
| Post PMI | 8.35* [0.40 - 16.30] | 1.16 [-7.64 - 9.97] |
| Post Global Fund | -5.26 [-14.94 - 4.42] | 4.55 [-6.02 - 15.12] |
| Post PEPFAR | -9.92 [-23.15 - 3.31] | 7.59 [-13.24 - 28.42] |
| No. observations (country-years) | 127 | 127 |
| Average in PMI countries before implementation | 10.6% | 39.9% |

| Panel B: DHS, AIS, MIS data (household-level) | Sensitivity analysis 2 – DHS data |
|---|---|
| | All children under-5 slept under net last night (household level) |
| | Coef. [95% CI] |
| *Implemented program* | |
| Post PMI | 13.1** [5.0 - 21.2] |
| Post Global Fund | -5.0 [-13.7 - 3.6] |
| Post PEPFAR | -7.0 [-15.7 - 1.6] |
| No. observations (household) | 410,261 |
| Average in PMI countries before implementation | 20.3% |

**Data sources:** The World DataBank: UNICEF, State of the World's Children, Childinfo, and Demographic and Health Surveys.
**Abbreviations**: Coef.=coefficient; 95% CI=95% confidence interval.
**Notes**: Coefficients can be interpreted as percent changes. All models also included country and year fixed effects. Robust standard errors were used to calculate confidence intervals and p-values. P-value notation: *** p<0.001, ** p<0.01, * p<0.05.

**Appendix 1 Figure A. Per capita disbursements for malaria from Global Fund and PMI over time**



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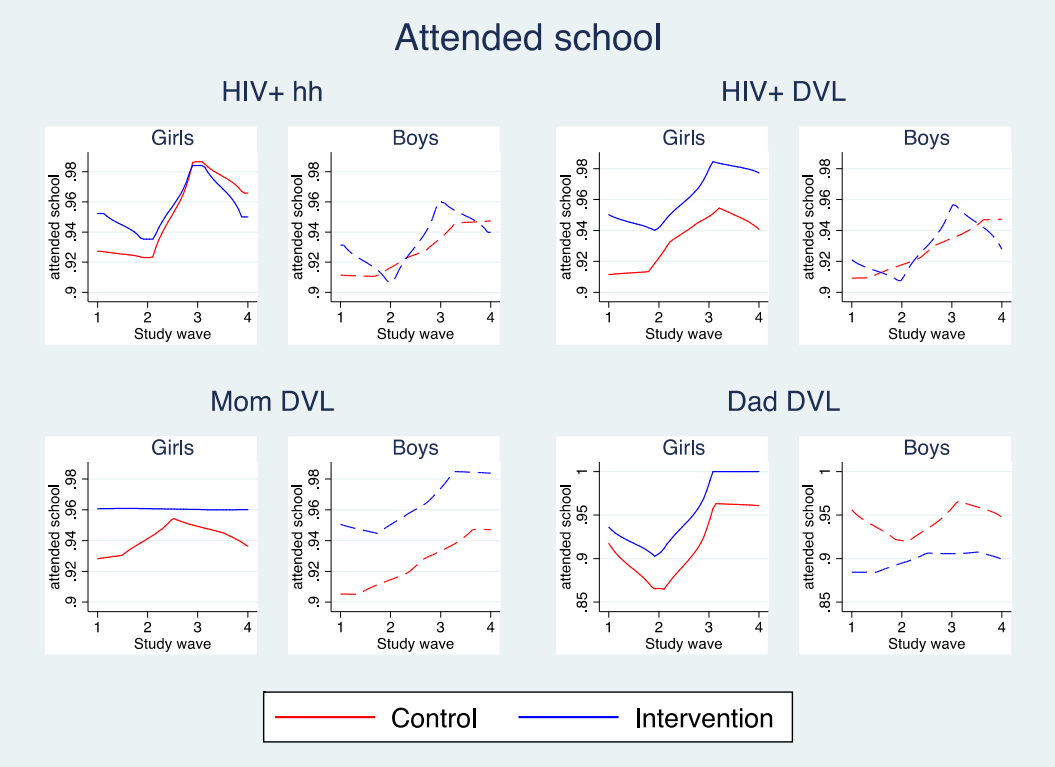
## APPENDIX 2: APPENDIX FOR CHAPTER 4

**Appendix 2 Figure A. Probability of school participation among boys and girls who were 9-16 years old at baseline in intervention and control communities over time**




**Abbreviations:** HIV+, HIV positive; DVL, detectable viral load; Study wave 0: baseline, 1: follow-up year 1, 2: follow-up year 2, 3: follow-up year 3.
**Note:** Trends were estimated using nonparametric kernel-weighted local polynomial regression (with Epanechnikov kernels and zero degree polynomials for local mean smoothing).

**Appendix 2 Table A. Impact of test-and-treat intervention on any school attendance last year among cohort of 9-16 year old children at baseline, by gender**

| Panel A: Boys | Full sample | Study group description | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | 0.01 | 0.02 | -0.00 | 0.01 | 0.01 | 0.03 | -0.02 | 0.13** |
| | (0.01) | (0.01) | (0.02) | (0.03) | (0.02) | (0.03) | (0.03) | (0.05) |
| Intervention * FUY2 | -0.00 | -0.01 | 0.00 | 0.01 | 0.02 | 0.03 | 0.02 | 0.02 |
| | (0.01) | (0.01) | (0.02) | (0.03) | (0.02) | (0.03) | (0.04) | (0.06) |
| Intervention * FUY3 | -0.01 | -0.02 | -0.00 | 0.04 | 0.01 | 0.08* | 0.05 | 0.12* |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.02) | (0.03) | (0.04) | (0.06) |
| Baseline mean | 0.940 | 0.954 | 0.921 | 0.915 | 0.928 | 0.930 | 0.931 | 0.927 |
| Observations | 7,446 | 4,447 | 2,999 | 1,398 | 2,084 | 912 | 569 | 343 |
| Number of id | 2,316 | 1,373 | 967 | 455 | 655 | 290 | 180 | 110 |
| Panel B: Girls | Full sample | Study group description | | | | | | |
| | | HIV status and viral load of adult in household | | | HIV status and viral load of biological parent | | Mother's viral load | Father's viral load |
| | | HIV- | HIV+ | DVL | HIV+ | DVL | DVL | DVL |
| Intervention * FUY1 | -0.02 | -0.02 | -0.01 | -0.04 | -0.02 | -0.02 | -0.07 | 0.04 |
| | (0.01) | (0.01) | (0.02) | (0.03) | (0.02) | (0.04) | (0.05) | (0.07) |
| Intervention * FUY2 | -0.02 | -0.03 | -0.02 | -0.02 | -0.03 | -0.02 | -0.07 | 0.05 |
| | (0.01) | (0.02) | (0.02) | (0.03) | (0.02) | (0.04) | (0.05) | (0.07) |
| Intervention * FUY3 | -0.03* | -0.02 | -0.05* | -0.03 | -0.05* | -0.03 | -0.05 | -0.00 |
| | (0.01) | (0.02) | (0.02) | (0.04) | (0.03) | (0.05) | (0.05) | (0.08) |
| Baseline mean | 0.947 | 0.952 | 0.94 | 0.933 | 0.941 | 0.941 | 0.945 | 0.936 |
| Observations | 6,928 | 4,125 | 2,803 | 1,241 | 1,778 | 739 | 441 | 298 |
| Number of id | 2,237 | 1,337 | 932 | 428 | 568 | 244 | 150 | 94 |

**Abbreviations:** HIV-, HIV negative; HIV+, HIV positive; DVL, detectable viral load; FUY1, follow-up year 1; FUY2, follow-up year 2; FUY3, follow-up year 3

**Notes:** Fixed effects linear probability models at the individual level control for underlying differences between children. Difference-in-differences models account for secular trends. Models also included controls for month of interview, school breaks and proportion of household members <18 years old. Standard errors in parentheses. Coefficients are interpreted as changes in probabilities. P-value notation: *** p<0.001, ** p<0.01, * p<0.05