Do it well or not at all? Malaria control and child development in Zambia

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Abstract

We assess the impact of recent large-scale anti-malaria efforts on child development in Zambia. Unlike the interventions examined in prior work on the human capital effects of malaria, the Zambian efforts led only to temporary reduction in exposure to the disease: in the most highly affected areas, parasite prevalence declined markedly in the two years after the beginning of the program scale-up, but resurged soon thereafter in highly endemic areas. Comparing cohorts born before and after the campaign launch, we find that children with initially low but resurgent malaria exposure perform more poorly on cognitive tests, and no better on anthropometric and executive functioning, than children from the same areas with high exposure in the first two years, and varying exposure after age 2. These findings are not explained by mortality or fertility selection, changes in parental investment, or crowd-out of other health services and behaviors. Instead, we hypothesize (and provide suggestive evidence) that the adverse results are driven by children's failure to form partial immunity to the disease in the first two years of life, making them more vulnerable to more severe illness when faced with resurgent disease. Our results suggest important tradeoffs between environment-driven early life developmental improvements and early life immunity development in models of human capital formation. They also suggest that sustained programmatic investment throughout childhood is critical to avoid potentially large adverse consequences of exposing non-immune populations to resurgent infectious diseases.

Keywords: human capital production; child development; cognition; malaria; eradication; immunity, adaptive responses; complementarity

JEL codes: I10, I14, I18, J13, J24

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1. **Introduction**

A growing body of work has demonstrated the importance of the *in utero* and early childhood developmental periods for the formation of cognitive and psychosocial skills (Sally Grantham-McGregor et al., 2007). Inadequate nutrition, infections, and a lack of cognitive stimulation during these periods can be detrimental to skill formation, both through hampering early endowment formation and lowering the returns to subsequent human capital investments (David J.P. Barker, 1992, Flavio Cunha and James J. Heckman, 2007, Peter Gluckman and Mark Hanson, 2006). Consequently, adverse early childhood environments can have negative impacts on well-being over the course of the life cycle, leading to lower educational attainment, lower lifetime wages, and poorer health outcomes (Douglas Almond and Janet Currie, 2011, Janet Currie and Tom Vogl, 2013).

In developing countries, infectious diseases are often a dominant feature of early childhood experience. Repeated exposure to high burden of infections harms developmental trajectories by reducing net caloric intake and absorption and by increasing systemic inflammation, both of which divert energy away from physical and mental growth (Christopher Eppig et al., 2010, Caleb Finch, 2007, Caleb Finch and Eileen Crimmins, 2006). Increased systemic inflammation can also impact neural architecture directly, undermining neurocognitive development (Jack P. Shonkoff et al., 2012, Phuong B. Tran and Richard J. Miller, 2003). In addition, infections may also adversely affect a child's ability to engage with, and learn from, their environment by reducing energy or creating social isolation.

A number of studies in the economics literature have demonstrated that early exposure to infectious diseases has long lasting consequences for adult schooling, labor market outcomes, as

well as adult health.[1] All of these studies use one-time adverse health shocks or interventions that produce long-lasting declines in disease risk to identify causal effects. However, temporary positive early life health shocks in environments where infectious diseases are endemic may have different consequences for human capital development. This is because, for certain infections, early exposure can result in partial immune response that helps protect individuals from developing severe illness later in childhood and through adulthood. Diarrheal disease, pneumonia, and malaria – the three leading causes of post-neonatal child mortality in the developing world (R. Lozano et al., 2013) – all demonstrate this pattern (Martin J. Blaser et al., 1985, William E. Collins and Geoffrey M. Jeffery, 1999, Ingrid Felger et al., 2012, B. P. Goncalves et al., 2014, Sunetra Gupta et al., 1999, Ralf Krumkamp et al., 2015, Ben Lopman et al., 2014, Ivo Mueller et al., 2013, R. R. Reves et al., 1989, E. Yang and B. K. Rubin, 1995).

Put differently, in endemic areas, interventions to reduce the risk of early life infectious diseases can delay the formation of partial immunity. From the perspective of human capital production, if children are permanently protected from the exposure (for example, due to the eradication of the disease), the failure to form partial immunity is not costly in the long run. If exposure reductions are only temporary, there may be a tradeoff between improved early life health and early immunity formation. In this latter case, the net effects of these competing forces on human capital development are not *a priori* obvious. On the one hand, one could argue that delaying the exposure to adversity beyond the first few years of life should benefit children, due to the particular importance of the first 1000 days for children's cognitive development (Sally Grantham-McGregor, et al., 2007). On the other hand, the first year of life is an important period where children are exposed to infection causing pathogens but often do not manifest severe

[1] See, for example, Almond (2006), Baird et al. (2012), Barham et al. (2013), Barreca (2010), Bhalotra and Venkataramani (2013, 2014), Bleakley (2007, 2010), and Cutler et al. (2010).

illness because of the protective benefits of proteins in maternal breast milk. Exposure to infections during this relatively protected period is critical in the formation of a robust response, given that the immune system's ability to identify, and adjust to, new pathogens is particularly high very early in life (Laura M'Rabet et al., 2008). Infectious diseases are often more severe after weaning and without partial immunity formed in early life, both the intensity of infection as well as the length of time over which the child faces severe infections may worsen considerably. This, in turn, could harm human capital formation.

Ultimately, the tradeoff between better early health and immunity formation for human capital production in resurgent disease environments is an empirical question. Answering it is more than just of academic interest, given the numerous instances of resurgence of infectious diseases like malaria in the context of weakening control programs (Justin M Cohen et al., 2012a) and the potential for changing infectious disease epidemiology due to climate change.

This paper examines this question in the context of Zambia's recent anti-malaria efforts. In Zambia, malaria accounts for 16% of deaths of children under the age of 5 (WHO, 2015), a figure which mirrors the burden faced in sub-Saharan Africa more generally.[2] To address this significant burden disease, Zambia initiated the Roll Back Malaria (RBM) program in 2006, with the intention of reducing malaria prevalence by 75% within 5 years. The program was initially successful, reducing the burden of malaria between 2006 and 2008 through a massive scale-up of insecticide-treated bednet distribution and indoor residual spraying (Nava Ashraf et al., 2010, NMCC, 2009). In 2009, program efforts came to a temporary halt due to disruptions of external funding inflows, with efforts resumed again in 2010. Despite the renewed, if not increased

[2] As discussed above, malaria is one of the major infectious diseases in developing countries. There are 200 million cases of acute malaria worldwide each year, resulting in one million deaths (see Murray, et al. (2012). Most of the morbidity and mortality from malaria is centered in sub-Saharan Africa (WHO (2010), Murray, et al. .

efforts, of the re-launched program, malaria incidence and prevalence did not continue to decline. Instead, they markedly resurged to levels close to the pre-intervention era.[3]

We estimate the impacts of early life exposure to RBM on developmental outcomes. We focus on program exposure during the first two years of life following evidence from the literature that this period confers the highest risk of adverse human capital outcomes.[4] Our data on developmental outcomes comes from the Zambia Early Childhood Development Project (ZECDP), a landmark study of 2,700 six-year-olds from the 2004 and 2006 birth cohorts (surveyed in 2010 and 2012, respectively) initiated to obtain a nationally representative assessment of children's skills prior to primary school entry. The Zambian Child Assessment Test (ZamCAT) battery, the core feature of the ZECDP, is one of the most comprehensive assessment of children in low and middle-income countries (Günther Fink et al., 2012). The battery assesses expressive and receptive language skills, general intelligence, working memory, executive functioning, as well as anthropometric measurements. In doing so, the survey captures a number of domains shown to be critical for human capital development in the psychology, education, and early childhood development literatures.[5] Importantly, in the ZECDP data, children born in 2004 were on average two years old when RBM was initiated, and thus largely exposed to malaria in the first 1000 days of their life, the most critical developmental period (Sally Grantham-McGregor, et al., 2007, Cesar Gomes Victora et al., 2010). Children born in 2006 may have been partially exposed in utero, but were at reduced risk of contracting malaria in

[3] The reasons behind the continued high burden of malaria are still poorly understood. While lack of funding likely explained the early resurgence, the persistently high malaria burden after the procurement of higher levels of funding after 2010 appears most consistent with parasite adaptation and resistance to bed nets and spraying as the two principal intervention strategies.

[4] See, for example, Barofsky et al (2011), Bleakley (2007), Cutler et al. (2010)(2010), Lucas (2010), Chang (2014) and Venkataramani (2012).

[5] See Cooper et al (2009), Dunn & Dunn (1981), Grantham-McGregor et al (2007), Grantham McGregor (2002), Smith Donald et al. (2007) and Wentzel and Asher (1995).

the first two years due to the initial impacts of RBM. However, they experienced resurgent malaria around the age of 3 and above.

To identify the causal effects of program exposure during the first two years of life, we follow Hoyt Bleakley (2010), David Cutler et al. (2010), Adrienne Lucas (2010), and others by utilizing spatiotemporal variation in malaria exposure at the sub-district (cluster) level generated by the Roll Back Malaria program. Our identification strategy rests on a continuous difference-in-differences framework, comparing cross-cohort differences in outcomes for children born in areas (clusters) with high versus low pre-intervention malaria parasite prevalence (MPP henceforth) levels. The relatively short time window we explore allows us to mostly rule out other long term regional or sub-regional changes co-moving with malaria exposure. Unlike the bulk of the literature on the human capital effects of malaria, the rich ZECDP data allows us to also directly assess early skill formation rather than relying on long-term human capital or schooling outcomes.[6]

Our core finding is that reducing early life exposure to infectious diseases may not always have a positive impact on early life cognitive development. Across all specifications, we find that in highly endemic areas, children born when malaria had temporarily dipped down due to the initial effect of RBM performed more *poorly* on cognitive tests than kids born in the same areas several years before the program started. We also look at physical (anthropometric) development and executive functioning, but do not find any impact of early exposure to RBM on those two domains. The differences for cognitive functioning were sizable: each 1 standard deviation decrease in malaria exposure was associated with a 0.2 standard deviation *decrease* in an index combining multiple cognitive test measures. These findings condition on cluster and

[6] The medical literature linking malaria to cognitive outcomes, which typically uses covariate-adjustment based-observational designs, is reviewed in Walker, et al (2007).

cohort fixed effects, measures of household income as well as parental characteristics and regional time trends.

We pursue and rule out a number of different explanations for this negative finding, including pre-existing trends, correlated time-varying area-level shocks, mortality and fertility selection, reduced supply (crowd-out) or demand for non-malaria related health services (such as vaccines), and changes in parental investments. In our view, the most likely explanation of the observed patterns is that children protected from malaria exposure through the early Rollback Malaria efforts in the first two years of life failed to form partial immunity to the disease, and, as a result, suffered from more severe infection when faced with resurgent malaria in their third and fourth years of life, undermining their ability to develop critical pre-school level skills.

We appeal to with a large body of evidence from the biomedical literature to support this hypothesis. This literature documents the importance of the first year of life for the formation of partial immunity as well as the importance of partial immunity for the prevention of severe illness in subsequent years (William E. Collins and Geoffrey M. Jeffery, 1999, Ingrid Felger, et al., 2012, Sunetra Gupta, et al., 1999, Ivo Mueller, et al., 2013) and the potentially disastrous effects of malaria rebound (R Romi et al., 2002). The same literature also suggests that early malaria infection is unlikely to result in severe cerebral malaria (which is most harmful for brain development) possibly due to the partial protection provided through maternal breastmilk (Bronner P. Gonçalves et al., 2014, Robert W Snow et al., 1997). In endemic settings, infection risks generally increases after weaning, while the risk of severe infection declines sharply thereafter due to immunity (Robert W Snow, 2015).

We also explore this hypothesis empirically. Using data from the Zambian Malaria Indicator Surveys, we show that the 2006 birth cohorts born in highly endemic areas experienced

lower infection rates and were less significantly less likely to report recent fevers or show biomarker evidence of anemia (both common consequences of malaria) in the first two years of life relative to 2004 cohorts born in the same areas. However, these cohorts were significantly more likely to report fevers and be anemic at the ages of 3-5.

One could interpret the overall patterns observed as evidence of health and health investment being more important at ages 3 and 4 (when the older cohort benefitted from the malaria efforts) than in the first two years of life. That is, the negative impacts could be less about the failure to form partial immunity, and more about the later the pre-school years being a relatively more sensitive period for the effects of health on human capital. While we cannot fully rule out this possibility in practice, the idea that later adversity should have a larger developmental impact is neither consistent with the general neuro-cognitive developmental trajectories (Sally Grantham-McGregor, et al., 2007), nor with a growing body of evidence finding largest developmental impacts for the first two years of children's life (John Hoddinott et al., 2008, Charles A. Nelson et al., 2007).

Our findings have a number of important implications. The idea that reduced early exposure to stressors can lead to more severe subsequent illness, is not only relevant to leading contemporary infectious causes of child morbidity and mortality, but is also consistent with a growing biomedical literature highlighting the importance of a broader set of adaptive responses to early life environments for long-run outcomes (Patrick Bateson et al., 2014, Jonathan C. K. Wells, 2012). In these models, fetuses and infants experience metabolic and epigenetic changes in response to cues about their current environment, which developing organisms take as proxy for the most likely future environments. If there is a mismatch between predicted and actual later life environment, the ensuing responses may be suboptimal and can cause harm in the long-term.

For example, in the context of nutrition, reduced nutrient availability *in utero* has been shown to be associated with a reduced ability to cope with abundant food supply in later life, with a substantially increased risk of later-life obesity (Xiaoping Lei et al., 2015, Ken K L Ong et al., 2000) and chronic disease (A. M. Sonnenschein-van der Voort et al., 2014). The inverse may also hold in some settings (though the evidence here is much more limited): relative abundance in the developmental years may be associated with poorer performance when faced with scarcity later in life (Patrick Bateson, et al., 2014).

Our findings are in line with this latter scenario: in the setting of recalcitrant, endemic malaria, temporary protection from malaria infection in early infancy may lead to maladaptation to the environment, with substantially reduced ability to cope with subsequent (resurgent) exposure. This cost of maladaptation is of course only relevant if changes in the malaria environment are not permanent, as it was the case in most settings studied in the prior work on the human capital consequences of early life malaria (Hoyt Bleakley, 2010, David Cutler, et al., 2010, Adrienne Lucas, 2010). Our findings pose a major challenge to major infectious disease campaigns: investments that seek to ameliorate infectious disease exposure can threaten both population health and child development if improvements in the disease environment cannot be sustained. This appears to be particularly relevant in the context of malaria control, which has been characterized by a long history of disease resurgence in the face of inconsistent funding, program implementation, and changes in disease ecology (Justin M Cohen et al., 2012b).

Our findings also have implications for the economics literature on human capital production. The argument that health or other human capital investments need to be sustained to achieve optimal skill formation has typically rested on appeals to dynamic complementarities in human capital inputs (Flavio Cunha and James J. Heckman, 2007, Flavio Cunha et al., 2010).

However, our results suggest that sustained investment may be critical for a second reason: temporal modifications in children's environment through external interventions may actually make children worse off if children become re-exposed to more hostile environments after the intervention.[7] Put differently, the dynamics of health investments and immunity formation that we across periods transcend constant elasticity of scale formulations of human capital development, at least for endemic infectious diseases. While CES models capture dynamic complementarity between investments over time, they do not necessarily capture mismatch. In addition, our findings models of human capital formation that consider the under-5 age range as a single developmental period, or focus on the first two years of life only, may not be a good approximation of early life developmental processes. Our results suggest that experiences at specific ages in the under-5 range can have a substantially different impact on children's developmental outcomes; they also suggest that these experiences are not independent, but rather co-dependent on children's environment in other period.

The rest of the paper is structured as follows. Section 2 describes the malaria eradication program in detail and Section 3 the data and measures. Section 4 presents the empirical strategy, Section 5 presents the main results and robustness checks. Section 6 examines explanations for our core findings and advances a case for our preferred case. Section 7 concludes.

2. Malaria Eradication in Zambia

Malaria is a parasitic disease spread by the *Anopheles* mosquito. The disease endemic in all parts of Zambia, with *Plasmodium Falciparum* by far being the most common parasite (as it is in the rest of sub-Saharan Africa). As seen in *Figure 1*, exposure to malaria (measured in terms

[7] With regards to worldwide malaria control, there are of course several other reasons for continued efforts including the risk of building resistance (Mendis et al., 2009).

of the fraction of children under 5 with evidence of parasites in blood samples, which we term as the malaria parasite positivity (MPP) rate, hereafter) in the year prior to the large-scale control efforts varied substantially across Zambia, with highest rates in the Northeast part of the country and the lowest rates in the Southwest. Malaria in Zambia is highly seasonal, peaking with the onset of the rainy season in December and leveling off with the arrival of the dry season in May. Between 2000 and 2005, malaria accounted on average for 48% of all under-5 inpatient visits, and for 30% of all under-5 mortality registered at inpatient facilities (Nava Ashraf, et al., 2010).

In 2006, Zambia started its anti-malaria efforts at large scale within the Rollback Malaria Partnership (RBM). The RBM campaign was designed as a national effort coordinated by the National Malaria Control Center and supported by a large group of international donors, including the Global Fund, World Bank, Bill and Melinda Gates Foundation, and the President's Malaria Initiative, with the ambition to reduce malaria by two thirds within five years (Zambia Ministry of Health, 2006). To date, the program remains one of the largest infectious disease treatment and prevention plans in per-capita-terms in the region, with an estimated annual budget of approximately US $10-15 per person/year. Between 2003 and 2010, the program received close to US $200 million in foreign contributions.[8] Following World Health Organization guidelines (WHO, 2005), the program's four principal strategies were (and continue to be): (1) administration of intermittent preventive treatment for pregnant women; (2) distribution of insecticide treated nets to all households; (3) indoor residual spraying; and (4) case management, including the systematic diagnosis of fever patients through Rapid Diagnostic Tests and their treatment with artemisinin-based combination therapies.

Large-scale program activities interventions started in 2006 and 2007, when the program received US$ 40 million of mostly external funding. As a result large reductions in the burden of

[8] See Mouzin et al. (2011).

malaria were seen between 2006 and 2008 (Nava Ashraf, et al., 2010, NMCC, 2009). *Figure 2*, which plots the regional and national prevalence of under-5 malaria between 2006-2012, illustrates the pronounced declines observed over the first years of the program. (As highlighted in Ashraf et al. (2010) the number of malaria inpatients remained relatively constant between 2000 and 2006 (with slightly higher rates in the 2001-2003 period), and then started to rapidly decline after 2006, coincident with the scale-up of Rollback Malaria – see *Appendix Figure 1*).

However, these impacts were short-lived. Program funding dropped markedly in 2009, as donor funding flows (*Appendix Figure 2a*) slowed in the wake of corruption issues at the Ministry of Health and a subsequent freeze of Global Fund funding (Ann Danaiya Usher, 2010, 2015). As a direct consequence, investment in anti-malaria efforts also dropped, and for example average per-capita distribution of ITNs in 2009 and 2010 per-capita distribution of ITNs was below the pre-RBM period (*Appendix Figure 2b*).[9] While funding levels were restored a year later, the same recovery was unfortunately not observed for malaria and child health indicators. As seen in *Figure 2*, the Zambia Malaria Indicator Survey (MIS) data in 2010 found resurgent MPP levels in virtually all high-endemicity areas. The resurgence was particularly pronounced in Eastern Province and Luapula, where MPP levels rose above 0.50 (meaning that half of children under-5 infected were infected at the time of the survey), while MPP levels remained relatively low in Lusaka, Northwestern and Southern Province. Nationwide, MPP was substantially higher in 2010 and 2012 than in 2008, and only slightly lower the (pre-program) 2006 levels. This was in spite of substantial declines achieved in six out of nine Provinces.

The exact reasons for the persistent reversal in trends in the most malaria exposed regions are still not well understood. The funding freeze in 2009 is likely only a partial explanation given

[9] Bednet distribution also declined in 2008, prior to the corruption scandal. This may be because bednets were expected to last 2-3 and thus cycles of provision were done at that interval. The lack of uptake in net provision in 2009 and 2010 is thus what we definitively link to faltering flows of funding.

that it was temporary. It is possible that partial (i.e., un-sustained) program efforts led to the natural selection of hardier mosquitos and parasites and, therefore, reduced efficacy of spraying and bed net coverage in these areas (Justin M Cohen, et al., 2012b). Both of these phenomena have been implicated in failures of control efforts in other contexts, as well (Pedro L. Alonso et al., 2011).

3. Data and Descriptive Statistics

The child development data used in this paper comes from the Zambia Early Childhood Program (ZECDP), which was launched in 2009 as a joint effort between the Harvard Center on the Developing Child, the University of Zambia, and UNICEF Zambia (Günther Fink, et al., 2012). The objective of the program was to generate a comprehensive assessment of children's development at the age of 6, just prior to school entry. For these purposes, a detailed child assessment tool was developed with a local expert team in 2010.

Two rounds of assessments were conducted in 53 clusters across six Zambian Provinces (*Appendix Figure 3*). The first round was conducted in 2010 focused on children born in 2004; the second assessment, conducted in 2012, focused on children born in 2006. Key domains of child development assessed were physical development, fine motor skills, receptive language, pattern recognition, spatial reasoning, and executive function. Physical development (height and weight) were measured using standard field kits. Receptive language, or an individual's ability to understand and process words, was measured by an adapted version of the Peabody Picture Vocabulary Test, a widely used assessment for this purpose (Lloyd M. Dunn and Douglas M. Dunn, 1997, 1981). Both a paper and an object-based version of the Kaufman Assessment Battery for Children (K-ABC) were used as a measure of pattern reasoning skills. Children were also completed a serial rapid automated naming test, where they were asked to identify the

names of a sequence of four familiar object symbols as fast as possible (Martha Bridge Denckla and LaurieE Cutting, 1999). The NEPSY block test (Marit Korkman et al., 1998) was used to assess spatial reasoning. To assess fine-motor-skills, children were asked to complete 10 basic locally adjusted tasks ranging from drawing basic figures to putting beads on a string and closing buttons on small dresses. Children also underwent a standard pencil (or peg) tapping test, testing for inhibitory control with and without distracting tasks (Adele Diamond and Colleen Taylor, 1996). Importantly, all of internationally validated tests were locally adapted with the help of local advisory team involving local researchers as well as members of the Ministries of Health and Education, and validated through two rounds of field-testing.[10] In addition to the developmental measures, the ZECDP also contains information on caregiver age, level of education, household wealth and assets, as well as a number of questions on child investments, such as the number of books in the household and enrollment in early childhood programs,

Data on malaria parasite prevalence (MPP) for under-5 children was obtained from the Zambian Malaria Indicator Surveys (MIS), which were implemented every two years from 2006-2012 by the Zambian Ministry of Health with technical assistance from international organizations such as the World Bank, the United States President's Malaria Initiative, UNICEF, and the World Health Organization.[11] Each survey consists of nationally representative household data[12] of the Zambian population, and includes information on spot malaria test positivity (based on laboratory confirmation of positive rapid diagnostic test results), hemoglobin measurements, and whether or not the household has been sprayed with insecticides or owns bednets. Roughly 2500-3000 children under 5 are surveyed in each repeated cross-section. The

[10] A more detailed description of the measurement tool development process and tool validity is provided in Fink et al. (2012) and Zuilkowski et al. (2012).
[11] See http://www.malariasurveys.org/.
[12] The Malaria Indicator Surveys follow a two-stage cluster sampling procedure, first randomly selecting census enumeration areas for the study, and then – after a full household listing in each area – randomly selecting households for the interview and biomarker collection.

ZECDP clusters were selected from the 120 clusters surveyed in the 2006 MIS: as such, we can calculate a pre-intervention cluster-specific MPP with the latter data. This serves as the main exposure measure.

Finally, we also use data from the 2007 and 2013 Zambia Demographic and Health Survey (ZDHS) to conduct key robustness checks. The 2007 ZDHS (Ministry of Health Central Statisctial Office, Macro International, (2007)) covers 6401 under-5 children born between 2002 and 2007 across all nine provinces of Zambia. Because it includes anthropometric (but not cognitive or personality) information on both the 2004 and the 2006 cohorts analyzed in this paper, these data will allow us to assess for pre-trends and correlated area-year shocks in ways that the ZECDP would not. The 2013 ZDHS (Ministry of Health Central Statistical Office, and ICF International. (2014)) covers 13,457 children under the age of 5; while does not cover the 2004 and 2006 cohorts per se, it does cover the ZECDP survey years of 2010 and 2012, which allows us to assess local changes in child outcomes between the two survey rounds.

Descriptive statistics for the ZECDP, MIS, and DHS surveys can be found in *Appendix Tables 1*, *2*, and *3*, respectively. In the ZECDP, sampling was restricted to pre-school age children, which means that most children are five or six years old. Just under half (48%) of children assessed were female. With respect to their physical development, children were on average one standard deviation below the reference median for height and 0.86 standard deviations below the reference median for weight. The cognitive development and inhibitory control measures were normalized to the pooled cohort. *Appendix Table 4* provides a correlation matrix of the developmental variables.[13]

[13] The overall correlation between physical and cognitive development scores is 0.22; the correlation between cognition and attention z-scores is 0.50.

In terms of broader household characteristics, average household size was 6.6, with an average caregiver educational attainment of 9 years, which corresponds to junior secondary schooling in Zambia.[14] Only 30% of households had any books for children, and less than half of caregivers reported that they ever read to children.

4. Research Strategy

Our empirical strategy rests on utilizing plausibly exogenous variation in early life malaria exposure generated by the national anti-malaria campaign to identify causal effects on child development. We operationalize this intuition by estimating a continuous difference-in-differences model (e.g., Bleakley, 2010, Cutler, et al, 2010, and Lucas, 2010), where we interact an indicator denoting children born around the time of the Rollback Malaria scale-up (i.e., the 2006 birth cohort) with baseline measures of malaria exposure in the MIS cluster of residence:

$$y_{ict} = \alpha_0 + \alpha_1 I_t^{Post} MPP2006_c + X_{ict}\beta + \gamma_t + \theta_c + \gamma_t \lambda_d + \varepsilon_{ict} \quad (1)$$

where *i* indexes the individual, *c* indexes the cluster of residence at time of the interview, *t* the birth cohort (2004 versus 2006), and *d* the district. I_t^{Post}= 1 for the 2006 cohort, who were exposed to successful Rollback Malaria in the first 2 years of life (*see Figure 3*) and *MPP* denotes cluster-specific malaria parasite prevalence rates in 2006. The vector ***X*** denotes child and family level characteristics at the time of survey, including household asset quintile, month of birth, gender, and caregiver education. The terms γ_t, θ_c and $\gamma_t\lambda_d$ refer to birth cohort, cluster, and cohort*district fixed effects, respectively. The child development outcomes are represented by *y*.

[14] Zambia's schooling system is divided into primary (grades 1-7), junior secondary (grades 8 and 9) and senior secondary (10-12) schooling.

We are interested in the coefficient on the interaction term (α_1), which denotes the difference in developmental outcomes across birth cohorts and areas with different malaria burdens. The key intuition is that areas with higher pre-intervention malaria burdens stood to benefit more from the control program. That is, if the malaria campaign was successful reducing early life malaria exposure and thereby improving child health and development, we should observe that children born in 2006 in areas of high malaria burden should particularly large improvements in child development compared to the children from the 2004 cohort born in the same villages; i.e., α_1 would be positive.

We formally test the assumption that areas with higher pre-intervention malaria burdens stood to gain more from Rollback Malaria, at least in the short-run, using data on child health and morbidity from the MIS. To do so, we utilize data from 2006 and 2008, just before and just after the program started to estimated models similar to (1), but look directly at malaria outcomes. Specifically, we examine malaria test positivity and anemia, which is common consequence of malaria infection (though is also related to nutritional intake and other comorbid conditions, such as hookworm infection).[15] If the program worked, we should see that morbidity outcomes improve between 2006 and 2008, and that these morbidity improvements are particularly large in the most highly endemic areas. Because the same clusters were not followed across MIS waves, we use district MPP as our exposure measure (there were 72 districts in Zambia in 2006).

As in most differences-in-differences models, identification hinges on there being no area- and cohort-specific shocks that are correlated with declines in malaria risk and developmental outcomes. For example, highly endemic areas may have experienced different

[15] Severe malaria is a function of serum hemoglobin. We follow the World Health Organization convention in defining age specific thresholds for anemia and severe anemia, respectively.

macroeconomic shocks or that they may have been differentially exposed to other health, education or welfare-related programs. To account for these possibilities, we include district X cohort fixed effects in our admin empirical model. Given that districts are the smallest administrative unit in Zambia, non-random sub-district variations in the exposure to government or NGO programming seem unlikely.[16] The inclusion of household wealth and caregiver characteristics additionally help control for potential cluster and year specific economic shocks that are unobserved in the data. We additionally address bias from unobserved shocks, as well as from pre-existing trends, measurement error, and mortality and fertility selection in the robustness checks below.

In terms of our outcome variables, we aggregated anthropometric and cognitive outcomes into a physical development index including weight, height, weight for height and a cognitive development index, comprising children's language, pattern recognition, fine motor skills, spatial reasoning, and rapid naming skills. The inhibitory control task serves as our single measure of executive functioning. These groupings follow recent work by Attanasio et al (2015). Within each domain, we use principal components analysis to create domain-specific index variables. The first principal component accounts for 65% of total variation in the physical domain and 36% of total variation in the cognitive domain.

Finally, to reduce bias in standard errors due to within-cluster dependence in outcomes over time (Marianne Bertrand et al., 2004), we cluster our standard errors at the cluster (ZECDP) or district level (MIS).

Results

[16] As discussed above, unlike the ZECDP, the MIS did not survey the same clusters from wave to wave, so we used MPP measured at the district level. Consequently, to account for area X cohort level confounders, we included province X year fixed effects.

5.1. Core Findings

Table 1 presents "first stage" results for immediate health outcomes among children under 2 years old in the 2006 and 2008 MIS. We find negative coefficients on the post*baseline MPP variable for all outcomes, which suggests that the program was indeed rather effective in reducing early life exposure to malaria and ill health. The results presented in Table 1 suggest that moving from the top to the bottom quintile of baseline parasitemia was associated with an 10% pt decrease (nearly 25% of the pre-intervention mean in high prevalence areas) in the probability of testing positive for malaria, a 22% pt decrease in the probability of severe anemia, and a 17% point decrease in the probability of having both fever and anemia, a symptomatology which is more specific (though not completely so) to malaria.

Figure 4 presents density plots for each of the three developmental domains, stratified by birth cohort and a dichotomized MPP variable (high if pre-program positivity > 20%, representing the upper quartile of the MPP distribution). For the lower prevalence clusters, we find rightward shifts of the distributions for each of the outcomes. In contrast, for higher prevalence clusters, post intervention cohorts actually appear to have *poorer* outcomes for each of the domains, with notable leftward shifts in the densities.

These results are confirmed when we include a full set of covariates and district-specific time trends in *Table 2* (estimates for each of the component measures are provided in *Appendix Table 5*). For the anthropometric index, we find small effects which are statistically indistinguishable from 0 (which is true for each of the component measures). However, for the cognitive index, we find a precisely estimated large, negative effect. This appears to be driven by the Kaufman and NEPSY tests (*Appendix Table 5*). The estimates imply a 0.2 s.d. decrease from a 1 s.d. decrease in baseline MPP. Put differently, moving to the top to the bottom quintile of

pre-program cluster malaria positivity rates implies -0.51 s.d. decrease in the cognitive index. Estimates on the inhibitory control test are also negative, implying a 0.3 s.d. decrease from a move from the top to the bottom quintile of cluster positivity, though this coefficient is not precisely estimated.

5.2 Robustness Checks

Here we discuss the results of a number of different robustness checks covering measurement error, outliers, omitted cluster-year shocks, and selection into the sample.

Measurement Error: This is a potentially important concern given that our cluster MPP measure is based on data from the MIS 2006, which surveyed a random sample of households from each of 53 clusters in our sample. On average, this measure is based on measurements for 15 under-5 children per cluster, opening up the possibility that our results might be biased towards the null by measurement error. That said, measurement error is unlikely to explain the large *negative* coefficients we find on cognitive outcomes.

Nevertheless, we address this issue in two ways. First, we replace our MPP measure with a cluster-specific measure of parasite incidence among children 2-10 years old derived from the Malaria Atlas Project (MAP) from 2005 (Simon I Hay and Robert W Snow, 2006). These data are constructed using community and population surveys on malaria parasite incidence (specifically focusing on *Plasmodium Falciparum*), using advanced interpolation techniques to provide high-resolution estimates of endemicity (S. Bhatt et al., 2015, Simon I Hay and Robert W Snow, 2006)[17]. Second, we instrument our MPP measure with the MAP measure. The results are presented in *Table 3*. Using the MAP measure (Panel A), we find large negative effects for each domain, with the cognitive aging being the largest and most precisely estimated. The results

[17] The MAP estimates are based on a mathematical model which builds on age-specific clinical incidence measured longitudinally at 30 sites. See Bhatt et al. (2015) for further details.

imply that a 1 s.d. decrease change in the MAP measure (0.1) is associated with a 0.14 s.d. decrease in the physical development index, a 0.67 s.d. decrease in the cognitive index, and a 0.23 s.d. decrease in the executive functioning measure. When using the MAP measure as an IV for the MPP measure (Panel B), we find larger magnitude impacts on the cognitive development measure compared to our main specification: a 1 s.d. decrease in MPP is now associated with a 0.36 s.d. in cognitive scores.

Outlier clusters: Given that malaria in Zambia is particularly high in specific regions, it is possible that marked swings in malaria prevalence or unobserved adverse disease or macroeconomic shocks in a few highly endemic areas could drive our main negative findings. To verify that our results are not driven by such outliers, we first estimate models that replace the continuous MPP variable with a binary indicator denoting baseline MPP in the upper quartile of the pre-intervention distribution (>0.25) versus below. This serves to group potential outliers with less extreme observations. The results, shown in *Table 3,* Panel C, are qualitatively similar to our core findings: moving from a high to a low malaria cluster (roughly 2 s.d. of the MPP distribution) is associated with a 0.4 s.d. decrease in cognitive skills. In *Figure 5*, we plot cross-cohort changes in each of the developmental domains at the cluster level as a function of the MPP levels observed in each cluster in 2006. As is clear from the figure, this correlation is to some extent driven by Luapula, the region where malaria resurgence has been most pronounced. To make sure the results are not just a reflection of this region, we exclude all Luapula clusters from our cross-cohort plots (Panel B of Figure 5). While the slope becomes a bit flatter, the relationship remains negative. Indeed, as seen in *Table 3*, Panel D, exclusion of the Luapula clusters from the regression does not change the substantive findings around cognitive

development and executive functioning, though the positive estimate on physical development reaches marginal statistical significance.

Omitted Area*Cohort or Area*Year Shocks: Omitted variable bias could arise from three related process. First, highly endemic areas, which tend to be located in Eastern and North-Eastern Zambia, tend to be poorer and less urbanized. It may be that such areas experienced distinct shocks to the macroeconomy or disease environment that coincided with the introduction of Rollback Malaria. Second, shocks that differentially affected the sample birth cohorts at any point after the Rollback Malaria campaign may bias the results, as well – the classic age-period-cohort problem. Finally, correlated pre-existing trends in developmental outcomes may have also drive the findings. A potential source of pre-existing trends is the increasing availability of antiretroviral therapy, whose reach expanded rapidly starting in 2004 (two years before the start of Rollback Malaria). The arrival of ART in associated was with improved survival and anthropometric outcomes (Adrienne M Lucas and Nicholas L. Wilson, 2013, Nicholas Wilson, 2014), among children in Zambia, and child human capital investment elsewhere (V Baranov et al., 2012).[18] Of note, for any of these processes to impact our results, they would have to be operative at the cluster*cohort level, as our models include district-cohort fixed effects.

We address the possibility of correlated cluster-level shocks in two ways. First, we estimate the same specification as (1) but this time use household socioeconomic characteristics as dependent variables. Finding large impacts on these indicators would suggest the possibility of

[18] HIV prevalence historically has been highest in the Southern districts, where malaria prevalence is generally low. As such, the clusters most likely to benefit from expanding access to HIV therapy are not the same clusters as those afflicted by malaria. The change in pre-existing trends in high HIV prevalence districts could be either positive or negative. If the effects on child human capital were dominant, we would expect that developmental outcomes were rising in what serve as "control" districts in our analysis, which would bias the estimates of malaria control impacts downward. This would have to be a massive effect given the large negative decline in developmental outcomes seen in high-prevalence districts. If the effects on selection were dominant, the bias would be in the opposite direction, since children with lower average human capital may increasingly be saved by HIV therapy in non-malarial district. However, as we argue below, this selection effect, too, would have to be unrealistically massive to bias the results we find.

important omitted factors.[19] As seen in *Table 5*, we do not find that to be the case. Second, we use the 2013 DHS to more closely investigate the hypothesis that the two cohorts were differentially affected by shocks in later years. Using these cohorts, we estimate versions of model (1) for anthropometric characteristics setting Post = 1 for the 2012 birth cohort and 0 for the 2010 cohort, choosing these two birth cohorts to match the ZECDP survey years. If the true process were driven by differences faced by exposure to malaria eradication in the first years of life, we would expect to see precisely estimated zero effects on anthropometric outcomes on each of these placebo cohorts. The idea is that this check can help rule out any macroeconomic shocks that occur may impact child development outcomes for the 2004 and 2006 outside of the infant and toddler window (and around the time the ZECDP was conducted). As seen in *Appendix Table 6*, we find no substantive or statistically significant coefficients on any of these indicators. These findings are consistent with the fact that, to our knowledge, there were no large-scale macroeconomic or environmental shocks that coincided with Rollback Malaria or the ZECDP surveys (indeed, 2006-2012 was a period of rapid economic growth in Zambia[20]).

To explore potential pre-existing trends, we used the 2007 DHS and regressed indicators of height and weight (the only developmental measures collected in this survey) against district MPP (given that the clusters are not the same as the ZECDP) interacted with birth cohort and district and birth cohort fixed effects, all for the 2003-2005 (pre-intervention) cohorts. As *Table 4* shows, we find no evidence in differential trends for these variables. In particular, these results suggest that the rapid expansion of HIV therapy starting in 2004 had little impact on our results.

[19] While we control for these indicators on the RHS in the main specification, if these are noisy proxies for relevant household circumstances, then it would be unlikely that they would impact the coefficient of interest in any significant manner. As such, placing these variables on the LHS is a reasonable way to assess whether family background shifts may have changed.

[20] The strong economic growth was apparent across all sectors of the economy, including agriculture (the dominant sector in the highly malaria endemic areas). Trends have been particularly positive after 2008, with annual growth rates consistently above 5% for the economy overall, and consistently over 10% for the agricultural sector (see *Appendix Figure 5*).

Mortality and fertility selection: A standard concern in the literature is that reduced mortality from positive health shocks may have increases the odds of survival of less developed or less resilient children, who may perform poorly on developmental assessments and bias the overall results (decreased selection). Conceptually, this scenario does not seem very likely given that the degree of mortality required for selection to overwhelm scarring (the negative but not fatal impact of an insult) is rather high (H. Alderman et al., 2011). In the Zambian case, under-five mortality at the time of the interventions was about 100 per 1000 live births (Zambia Central Statistic Office et al., 2009), with an estimated 20-25% attributable to malaria (GBD Collaborators, 2014). Given these numbers, reducing malaria mortality by 50% would thus have increased the percentage of children surviving from each cohort from 90 to 91.25% at most; even if this group of children has an average z-scores of -2, the maximum plausible shift in population average outcomes would have been smaller than 0.03 SD, which is nowhere close the magnitudes observed in *Tables 2* for cognitive development.

The extent to which fertility selection plays a role depends on the extent to which the price of child quality fell relative to that of quantity and whether the fertility response differed across families in the ability distribution. If, as in Lucas (2013), the quantity price effect is dominant, then an increase in the number of low quality children may explain the negative findings. However, again, this effect has to be large to explain our profoundly negative findings, which is not consistent with the overall trends observed: according to the 2013 DHS, total fertility rates declined only marginally at the country level from 6.2 in 2007 to 5.3 in 2013, with no consistent differences across provinces. In addition to this reasoning, *Table 5*, where we consider the caregiver and household socioeconomic characteristics as dependent variables does not suggest a shift towards low quality parents.

6. Mechanisms

As shown in the previous sub-section, our negative findings are unlikely to be explained by omitted cluster-year level processes or shocks, mortality, or fertility selection. In this section, we explore additional mechanisms behind our findings.

6.1. Unlikely Explanations

One possible explanation for the empirical patterns observed in our data is that health adversity at age 3 has a bigger impact on child development than health adversity in the first two years. In practice, we are comparing only two cohorts in our data, and the younger cohort (children born in 2006) had lower exposure to malaria in the first 2 years, but higher exposure to malaria at ages 3 and 4 than the older cohort. While it is possible in principle that health at older age is more important, this finding would be in stark contrast to pretty much the entire literature in this field, which has consistently highlighted the first 2 years (or first 1000 days) of children's life as the most sensitive period with respect to malaria exposure (Alan I. Barreca, 2010, Hoyt Bleakley, 2010, Adrienne Lucas, 2010, Atheendar Venkataramani, 2012). Even if it is likely that poor health at older ages undermines children's potential development, it would be rather counterintuitive if these effects were substantially larger than the benefits created by an equally-sized reduction in health adversity earlier on in life when a majority of brain functions are developed (Sally Grantham-McGregor, et al., 2007).

Along similar lines, one may argue that the findings could be driven by negative income shocks from child or adult malaria in during the resurgence years. However, for this explanation to hold, the marginal effect of household income on endowment formation and developmental outcomes would need to be higher for pre-schoolers rather than infants or toddlers. The literature

on the long-run effects of income shocks does not support this contention (Abhijit Banerjee et al., 2010, Sharon Maccini and Dean Yang, 2009).

Another potential explanation involves parental investments that respond to the malaria health shock; that is, pre-eradication infants may have received greater human capital or health investments by virtue of being sicker early in life. While the weight of the literature suggests that human capital investments tend to be reinforcing (Douglas Almond and Bhashkar Mazumder, 2013), some new evidence suggests that subsequent health investments may serve a compensatory purpose (Junjian Yi et al., 2014). However, *a priori* the potential of compensating investments explaining the negative findings in this study seems unlikely as it would suggest compensation of pre-eradication cohorts to a degree that goes above and beyond what seems expected in the literature (Douglas Almond and Bhashkar Mazumder, 2013).

A third potential mechanism is that malaria eradication programs may have reduced the demand for, or crowded out the supply of, preventative services such as vaccines. A recent line of work in the economics literature documents the potential importance of this mechanism. For example, Daniel Bennett (2012) demonstrates an increase in diarrheal disease rates after the provision of piped water due to over-compensatory behavioral responses in sanitation disposal. Pinar Keskin, et al (2013) use data from Bangladesh to demonstrate a reduction in breastfeeding by parents in response to improvements in groundwater arsenic content, potentially leading to increases in infant mortality, as well. Karen Grepin (2012) and Nicholas Wilson (2015) provide suggestive evidence of crowd out of child vaccination with scale-up of HIV treatment services in sub-Saharan Africa, the only global health program larger in scope than Rollback Malaria.

In order to test the relevance of both the parental investment and demand for/supply of health care explanations for our findings, we estimate our core model using data on parental

effort and investments from the ZECDP and DHS as dependent variables. The ZECDP data allows us to examine impacts on parental inputs, which include whether parents currently spend time reading to their children, whether the household has children books, whether the household has other reading material, the number of years the child was allowed to attend (generally rather costly) early childhood development centers, and retrospective information on the length of breastfeeding. The DHS data allows us to look at breastfeeding duration and parental vaccination behaviors, which captures both health investment and resource crowd-out.[21]

Table 6 shows the main results from this analysis: while the interaction between post and MPP is consistently negative for all ZECDP and DHS measures, none of the estimated coefficients is significant.

6.2. Partial Immunity and Resurgent Disease

Having ruled out a number of competing possibilities, we argue that the most likely explanation for our findings is lack of malaria exposure in early life may increase vulnerability to the disease in later childhood. A large literature has documented the importance of partial immunity formation in early childhood (William E. Collins and Geoffrey M. Jeffery, 1999, Ingrid Felger, et al., 2012, Sunetra Gupta, et al., 1999, Ivo Mueller, et al., 2013). In general, immunity is formed as a result of disease exposure during the breastfeeding period. This immunity is partial because, while it does not prevent individuals from acquiring the disease, it does reduce the severity of illness. Because breast milk appears to protect infants from (severe) malarial infection, partial immunity initially develops during a "protected period" (Denise L. Doolan et al., 2009, Robert W Snow, et al., 1997). The dynamics of immune system responses to

[21] While a number of vaccines are reported in the DHS, we focus on BCG and polio: both vaccines are supposed to be administered in the first six months of life, which means that we can more readily compare children from the 2004 cohort to children from the 2006 cohort, who were on average only 12 months old when the 2007 DHS was conducted.

malaria and breastfeeding are thought to explain the unique epidemiologic profile of the disease in endemic regions among children under the age of 5: while exposure to parasites (and bloodstream presence of parasites) remains constant, the risk of severe disease increases right after weaning and then declines sharply thereafter (B. P. Goncalves, et al., 2014).

With regards to this study, cohorts born in 2004 in high-endemicity areas experienced a higher risk of malaria exposure during infancy than their post-intervention counterparts, and were thus more likely to form partial immunity. By 2006, when Rollback Malaria was being scaled up, these pre-intervention cohorts were at an age where further episodes of malaria were less likely to be severe given their partial protection. In contrast, intervention birth cohorts faced little malaria in the first two years of life, but resurgent disease thereafter. Following the partial immunity hypothesis, these cohorts may have consequently faced more frequent and much more severe disease during the pre-school years.[22] In fact, the overall under-5 burden of disease may have been *higher* for the 2006 birth cohorts as a result of resurgence. This would explain why the impacts we recover on developmental outcomes are so profoundly negative.

Unfortunately, there is no direct test of the partial immunity hypothesis that is possible with our data (which would require biomarker data on immunoglobulins). We instead embark on an indirect test. The partial immunity hypothesis we outline predicts that (1) individuals born in endemic regions after RBM would be less likely to test positive for malaria in the first two years of life, due to successful campaign efforts, and equally likely to test positive as 3 and 4 year olds compared to pre-intervention birth cohorts, and (2) malarial infections would be much more severe for post-intervention birth cohorts in endemic areas exposed to malaria at age 3 and 4

[22] Several recent studies show that reducing exposure to early malaria through interventions can delay immunity acquisition and increase incidence at older ages (Konaté, et al. (2011), Guinovart, et al. (2012), Aponte, et al. (2007). Delayed immunity acquisition does however not mean that the overall burden of ill health is higher, even if malaria episodes occur later in life. One plausible explanation is that episodes of malaria experienced are more severe (and more likely to result in cerebral malaria) as suggested by Doolan et al (2009).

because of the lack of partial immunity to quell symptoms. We have already shown in *Table 1* that malaria test positivity and anemia was lower for the 2006 birth cohort during the first 2 years of life. We can use the MIS data from 2008 and 2010 data to estimate similar models, this time focusing on preschoolers (3-5 year olds).[23]

The results are presented in *Table 7*. Consistent with the immunity model predictions, we find small to no effects of early exposure to Rollback Malaria on malaria test positivity rates. However, we do find that children exposed to Rollback Malaria had much lower serum hemoglobin measures and significantly higher risk of having severe anemia, as well as concurrent fevers and anemia (which is more specific to malaria exposure). The coefficient pattern in *Table 7* is striking in that the signs are exactly opposite as those in *Table 1*, which examined the impacts of Rollback Malaria exposure on infants and young children. While it is not obvious from a casual glance at the coefficients, the results in *Table 7* imply that program impacts on malaria related outcomes at age 3-5 were more severe than the initial benefits of a disease free environment. For example, the results from *Table 1* imply that a 1 s.d. temporary decrease in birth cohort MPP was associated with a decrease in severe anemia equivalent to 64% of the age 0-2 mean, but a 75% increase relative to the age 3-5 mean.

For all of these analyses, it is important to rule out local changes in access to malaria prevention and therapy, which would serve as a competing explanation for the partial imunity hypothesis. Specifically, for changes in malaria control activity to explain our results, we would have to find that cohorts affected by Rollback malaria in the first years of life were exposed to reduced prevention and treatment efforts at ages 3-5. This seems unlikely because the resumption of Rollback Malaria programmatic spending would have likely increased access to these services

[23] As before, the cluster across different MIS waves changed between 2006 and 2010, so we use district MPP rates in 2006 as our baseline exposure.

in affected clusters at the time of survey. The MIS data contain information on household ownership of insecticide treated bed nets and whether the household received insecticide spraying. Consistent with our priors, we find increases in the likelihood that households of 3-5 year olds who were exposed to Rollback Malaria early in life owned an insecticide treated bed net and received spraying, though the coefficients are not precisely estimated (*Appendix Table 7*). We also do not find any negative impacts on the availability of anti-malaria therapy.

7. Discussion and Conclusion

Over 200 million children in the developing world are thought to be at risk of not meeting their developmental potential (Sally Grantham-McGregor, et al., 2007). Many of these children reside in sub-Saharan Africa, where malaria remains a leading cause of child morbidity and mortality. Using quasi-experimental methods, we demonstrate a robust link between these two phenomena, suggesting that public health efforts to eradicate malaria worldwide may help unleash the economic potential of a sizeable portion of the future global workforce. This contention supports several recent studies showing the human capital benefits of early exposure to malaria eradication efforts (Hoyt Bleakley, 2007, David Cutler, et al., 2010, Adrienne Lucas, 2010).

However, compared to most of this recent literature, our results are much more nuanced, and suggest that efforts to control malaria may not always be beneficial for children. We find that in the Zambian context, early life exposure to malaria control efforts led to *worse* cognitive development, with no impacts on physical development or inhibitory control. We attribute this result to the fact that the program was only temporarily successful, which is unfortunately a common occurrence in malaria control though a situation not well explored in the economics

literature. Even though resurgent malaria should have affected both younger and older children in our sample, it seems that the environmental changes observed between 2006 and 2010 were much more harmful for those initially exposed to successful malaria control in the first 2 years of life. Ruling out other explanations, we argue that this cohort failed to acquire the partial immunity needed to fend off more serious infections in ensuing years. Consequently, when malaria re-emerged in 2009, the health impact was much larger for this younger cohort than for older children from the same communities. The policy implications of this are rather obvious: temporary malaria control efforts will inevitably result in resurgence (Justin M Cohen, et al., 2012b), and may cause harm in excess of the progress initially made as populations lose immunity (Flemming Konradsena et al., 2004) .

The adaptive behaviors – specifically the molecular changes involved in immunity formation - which we believe underlie our findings have important implications for human capital formation. First, the relevance of such processes in early childhood implies a production function whose properties transcend simple cross-period substitution and dynamic complementarity. That is, our results suggest that mismatches between early and later environments can produce outcomes that may be worse than continued exposure to high or low risk environments. This finding is consistent with theories from the biomedical sciences and evolutionary biology premised around early responses to nutritional and inflammatory cues. While these environments generate responses that are adaptive in the short run (to ensure reproductive success), changes in the environment later in life may render them maladaptive (David J.P. Barker, 1992, Peter Gluckman and Mark Hanson, 2006). As one variant of this general model, the Predictive Adaptive Response (PAR) hypothesis, postulates, "*mismatch[es] between the individual's phenotype and the conditions in which it finds itself can have adverse*

consequences for Darwinian fitness and, later, for health." (Patrick Bateson, et al., 2014, page 1)

Models of adaptive responses in human capital development provide an alternate rationale for multi-period investments beyond dynamic complementarity. We argue that theoretical models of human capital formation should take these biological mechanisms into account. While our paper presents one specific example of how biological mechanisms may matter, from a policy perspective it is not a trivial one: malaria is incredibly common in the developing world. Moreover, the findings may extend to other common infectious diseases, such as diarrhea and pneumonia,[24] as well as health and nutritional investments, given the potential general relevance of models of predictive adaptive responses in explaining developmental phenomena.

Our results also highlight the importance of understanding the dynamics within the broad period of what constitutes "early childhood." Complementarities within the first years of life are consequential, suggesting that this time of life cannot be considered a single developmental period. Along these lines, our findings also highlight the importance of child development beyond the first 1000 days of children's life: even though the first 1000 days are of critical importance for early skill formation and epigenetic adjustments, the impact of these early experiences on adult outcomes can likely only be understood through a comprehensive assessment and targeting of children's later childhood and teenage experiences.

[24] See Reves, et al. (1989), Blaser, et al. (1985), Krumkamp, et al. (2015), Lopman, et al. (2014), Yang and Rubin (1995).

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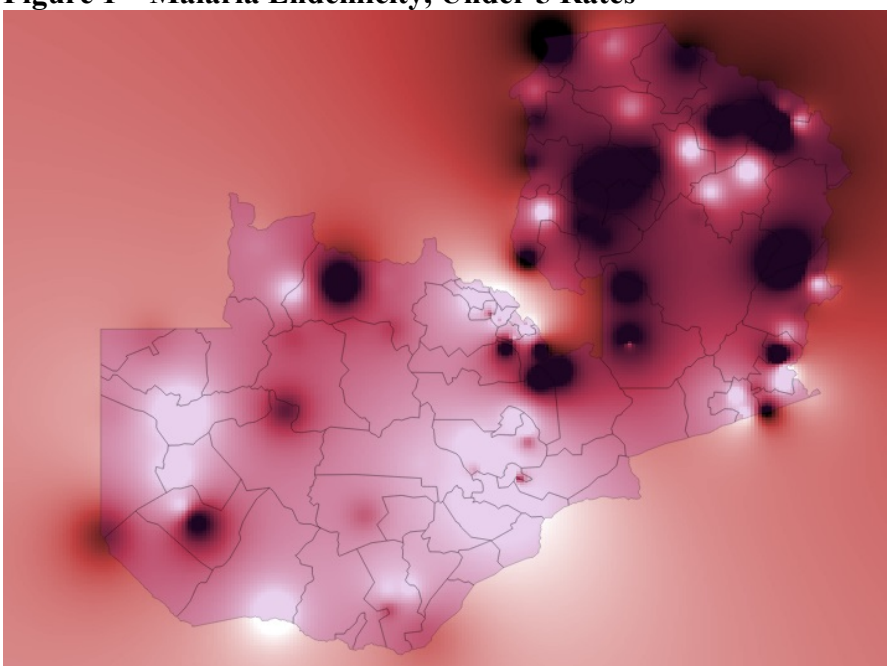
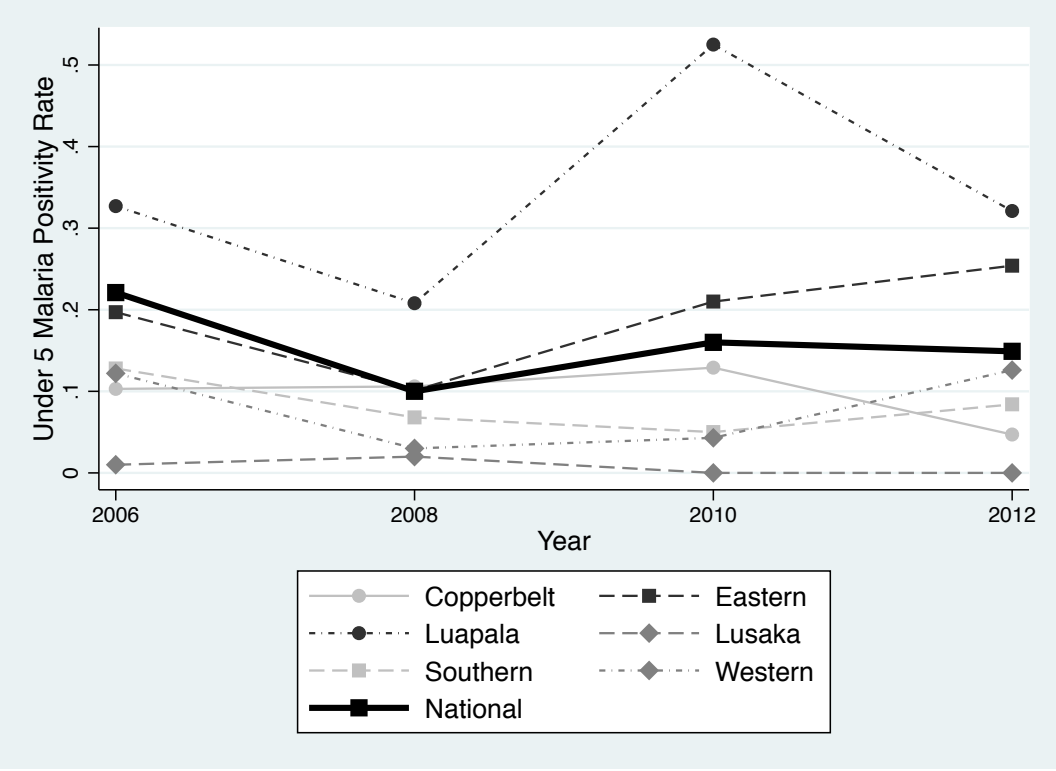
Figure 1 – Malaria Endemicity, Under 5 Rates



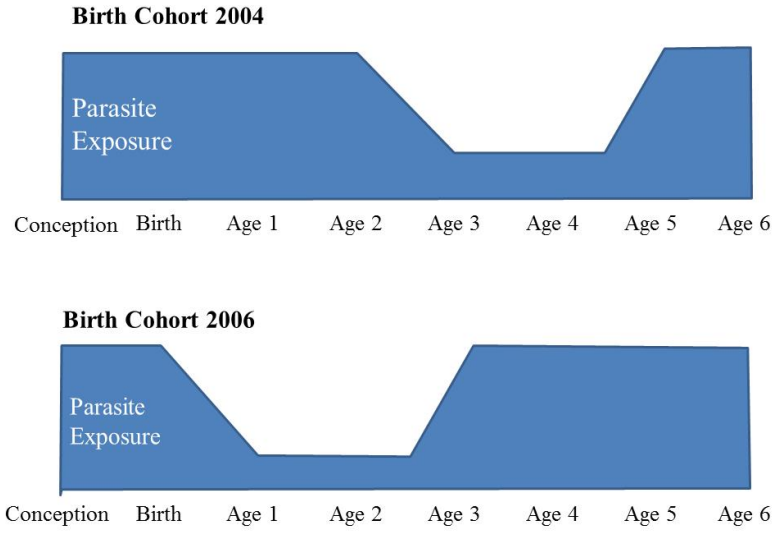
Notes: Data from Zambia Malaria Indicator Survey, 2006. Inverse-distance weighted spatial interpolation of 120 study cluster observations used to predict local malaria parasite positivity (MPP) rates among children 5 and under. White corresponds to an MPP of zero; the darkest areas correspond to an MPP of 0.5 (i.e., 50% of surveyed children tested positive for parasites in the bloodstream by a rapid diagnostic test).

Figure 2 – Trends in Malaria Infection Rates, 2006-2012



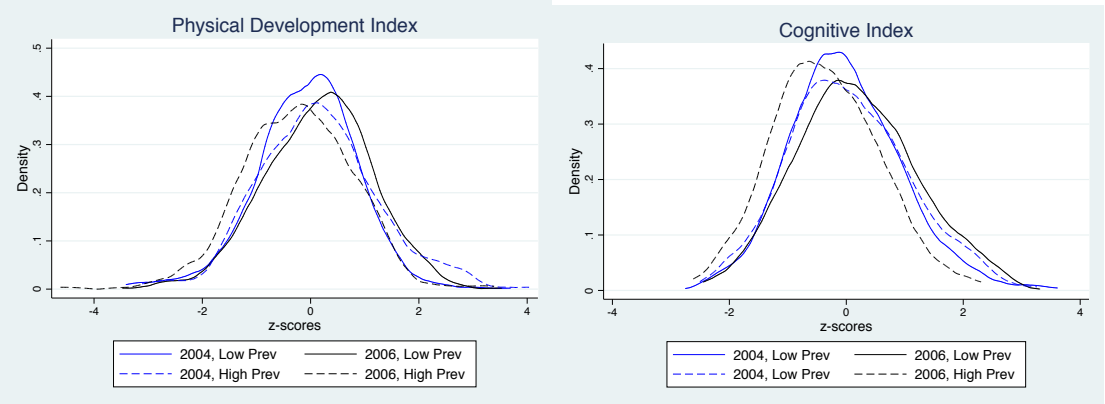
Notes: Data from Zambia Malaria Indicator Surveys, 2006-2012. Provinces displayed are those represented in our child development sample. Focusing on the national trend line, the figure shows a drop in under-5 malaria rates by 50% between 2006 and 2008, with resurgence in 2010. In the high prevalence Eastern and Luapala provinces, parasite positivity rates in 2010 actually exceeded those in 2006.

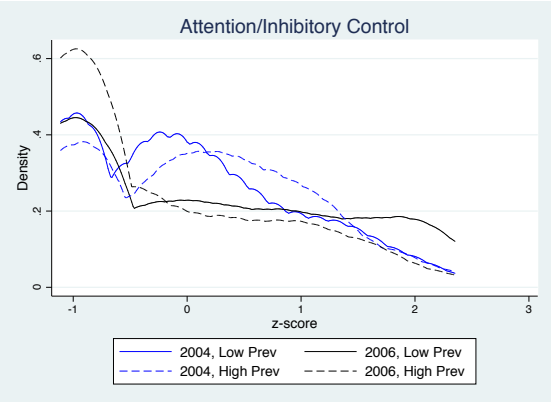
Figure 3: Cohort Differences in Malaria Exposure in Highly Endemic Areas



Notes: Schematic plotting prevailing malaria prevalence (and thereby risk of infection) by age for each birth cohort in the ZECDP sample. The 2006 cohort was exposed successful, but temporary, control efforts in the first 2 years of life, while the 2004 birth cohort was exposed to the improved disease environment at age 3-4.

Figure 4 – Density Plot of Developmental Outcomes

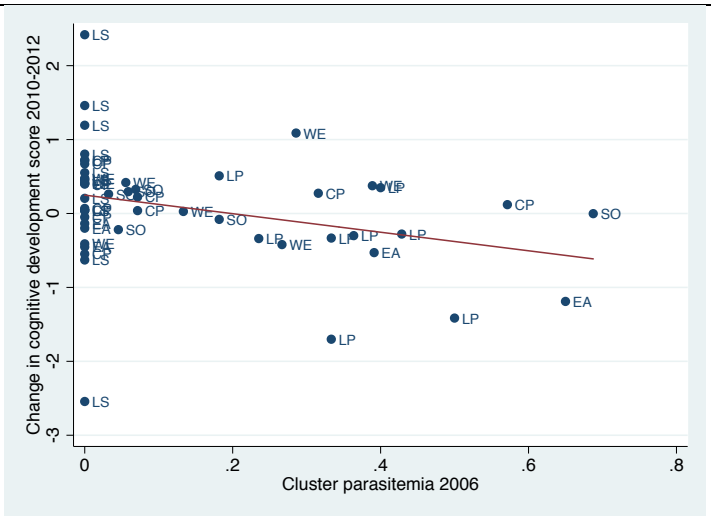




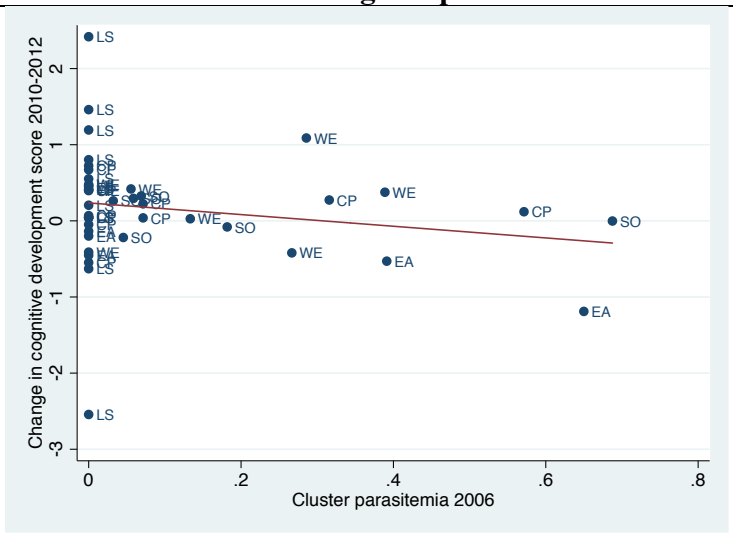
Notes: Figures plot densities of physical and cognitive indices and executive functioning test z-scores for each ZECDP birth cohort. Plots stratify by residence in a cluster with high versus low under-5 malaria prevalence at baseline, which is determined based on MPP above or below 0.2. For all outcomes, we find developmental outcomes *worsened* for cohorts born in 2006 in high prevalence areas. In contrast, in low prevalence areas, outcomes appear to have improved.

Figure 5: Cluster-level Changes in Cognitive Development and 2006 MPP Levels

Panel A: All 53 Clusters



Panel B: Excluding Luapula Clusters



Notes: Each graph plots the difference in average cluster*birth cohort-specific cognitive index z-scores against cluster MPP in 2006. The province within which each cluster resides is labeled as follows: CP = Copperbelt, EA = Eastern, LU = Luapala, LS = Lusaka, SO = Southern, WE = Western.

Table 1 – Rollback Malaria Exposure and Malaria Outcomes at Ages 0-2

	Positive Malaria Test	Hemoglobin	Anemia	Severe Anemia	Fever and Anemia
Post * MPP	-0.233*	2.580***	-0.224*	-0.480***	-0.379**
	(0.134)	(0.533)	(0.130)	(0.0935)	(0.181)
Observations	1,819	1,780	1,780	1,780	1,370
R-squared	0.192	0.174	0.125	0.125	0.143

Notes: Estimates of model (1) in main text, using biomarker data from the 2006 and 2008 Malaria Indicator Surveys. All models control for age and sex of child, and include district, survey year, cohort, province*survey year, province*cohort fixed effects. Robust standard errors, corrected for clustering at the district level, in parenthesis. Sample includes all children under the age of 2 who were born between 2004 and 2007. Post = 1 for the 2006 and 2007 birth cohorts, and 0 otherwise. MPP reflects the district specific under-5 malaria test positivity rate in 2006. ** p<0.01, ** p<0.05, * p<0.1.

Table 2- Rollback Malaria Exposure and Developmental Indices

	Physical Development Index	Cognitive Development Index	Attention/ Inhibitory Control
Post * MPP	0.0943	-1.130**	-0.687
	(0.258)	(0.450)	(0.565)
Observations	1,815	2,101	2,307
R-squared	0.217	0.352	0.322

Notes: Estimates of model (1) in main text. All models control for household wealth quintile, age and sex of child, caregiver education, and include cluster, cohort, and district*cohort fixed effects. Robust cluster corrected standard errors are in parenthesis. Physical and Cognitive Development Indices are derived from principal component analyses (see main text and Appendix Table 1). Estimates for component test scores are provided in Appendix Table 5. *** p<0.01, ** p<0.05, * p<0.1.

Table 3 – Robustness Checks, Impacts on Developmental Indices

	Physical Development Index	Cognitive Development Index	Attention/Inhibitory Control
Panel A - Alternate Baseline Malaria Measure			
Post * MAP Falciparum Endemicity	-1.443	-6.772**	-2.376
	(2.717)	(2.591)	(4.594)
Observations	1,815	2,101	2,307
Panel B - Instrumental Variables			
Post * MPP	-0.181	-1.923***	-0.142
	(0.597)	(0.592)	(1.165)
First Stage F-Statistic	13.99	9.61	15.13
Observations	1,815	2,101	2,307
Panel C - Discrete Exposure Variable			
Post * High Prevalence	0.122	-0.400*	0.114
	(0.137)	(0.225)	(0.278)
Observations	1,815	2,101	2,307
Panel D - Remove Luapula Clusters			
Post * MPP	0.302*	-1.291***	-1.041
	(0.166)	(0.406)	(0.691)
Observations	1,486	1,750	1,915

Notes: Robustness checks of models in Table 2. All models include controls for household wealth quintile, age and sex of child, caregiver education, and cluster, cohorto, and district*cohort fixed effects. Robust cluster corrected standard errors are in parenthesis. *** p<0.01, ** p<0.05, * p<0.1.

Panel A replaces our core MPP measure with cluster specific measures of Plasmodium Falciparum positivity from the Malaria Atlas Project (MAP). In Panel B, we use the MAP measure as an instrument for MPP in 2SLS models. In Panel C, we replace MAP with a binary indicator of high prevalence, which = 1 for clusters in the upper quartile of the MPP distribution (MPP>0.25) and zero otherwise. The mean MPP for clusters where High Prevalence = 1 is 0.41; it is 0.045 for the remaining clusters. In Panel D, we estimate our core model (as in Table 2), but this time excludes all districts in the Luapula province, where malaria endemicity is the highest in Zambia.

Table 4 – Pre-Existing Trends in Child Health and Development

	Fever	Stunted	Underweight	Wasted	Child death
Time * MPP	0.0366	-0.0858	-0.0117	-0.00491	0.0692
	(0.0817)	(0.0962)	(0.137)	(0.0715)	(0.0614)
Observations	3,823	3,077	3,077	3,077	3,823
R-squared	0.147	0.162	0.141	0.128	0.098

Notes: All models control cluster fixed effects, cohort fixed effects as well as region-specific time trends. Robust standard errors are clustered at the district level. Sample includes all children born between 2003 and 2005. MPP reflects the district specific under-5 malaria test positivity rate in 2006. Fever represents fever prevalence in 2 weeks preceding survey. Stunted, underweight and wasted are defined as HAZ, WAZ and BMIZ < -2. *** p<0.01, ** p<0.05, * p<0.1.

Table 5 – Tests of Sample Composition Changes, Rollback Malaria Exposure and Household Characteristics

	Household Size	Household Asset Score	Wealth Quintile	Caregiver Schooling (Years)
Post * MPP	0.822	-0.187	0.0394	-0.320
	(0.693)	(0.640)	(0.648)	(1.699)
Observations	2,392	2,426	2,426	2,326
R-squared	0.263	0.568	0.553	0.341

Notes: Estimates of model (1) in main text. All models include cluster, district, cohort, and district*cohort fixed effects. Robust cluster corrected standard errors are in parenthesis. Household Asset Score is a Filmer-Pritchett Index based on household ownership of a number of durable and consumer goods. *** p<0.01, ** p<0.05, * p<0.1.

Table 6 – Rollback Malaria and Parental Investments

	Adults Reads to Child	HH Has Children's Books	HH Has Other Books	ECD Program (Years)	BCG Vaccine	Polio Vaccine	Length of Breastfeeding
Post * MPP	0.475	-0.290	-0.142	0.104	0.0665	0.0764	1.425
	(0.303)	(0.210)	(0.196)	(0.634)	(0.0644)	(0.0618)	(1.415)
Observations	2,322	2,322	2,322	2,271	2,423	2,423	2,593
R-squared	0.228	0.232	0.297	0.356	0.211	0.189	0.448

Notes: Estimates of models examining parental investments. Robust cluster corrected standard errors are in parenthesis. Adult Reads to Child, HH Has Children's Books, HH Has Other Books, and ECD Program (which denotes the number of years a given child spent in preschool or an early childhood program) are all derived from the ZECDP. For these variables, MPP is defined at the cluster level and all models include the controls listed in Table 2. BCG Vaccine, Polio Vaccine, and Length of Breastfeeding (in months) are derived from the 2007 DHS. The DHS sample is restricted to the two main study cohorts, i.e. children born in 2004 and 2006. Polio is coded as one if the child got at least one polio vaccination. Breastfeeding refers to the nuber of months the child was exclusively breastfed. Columns 4-6 include cluster fixed effects as well as regional-specific time trends. *** p<0.01, ** p<0.05, * p<0.1.

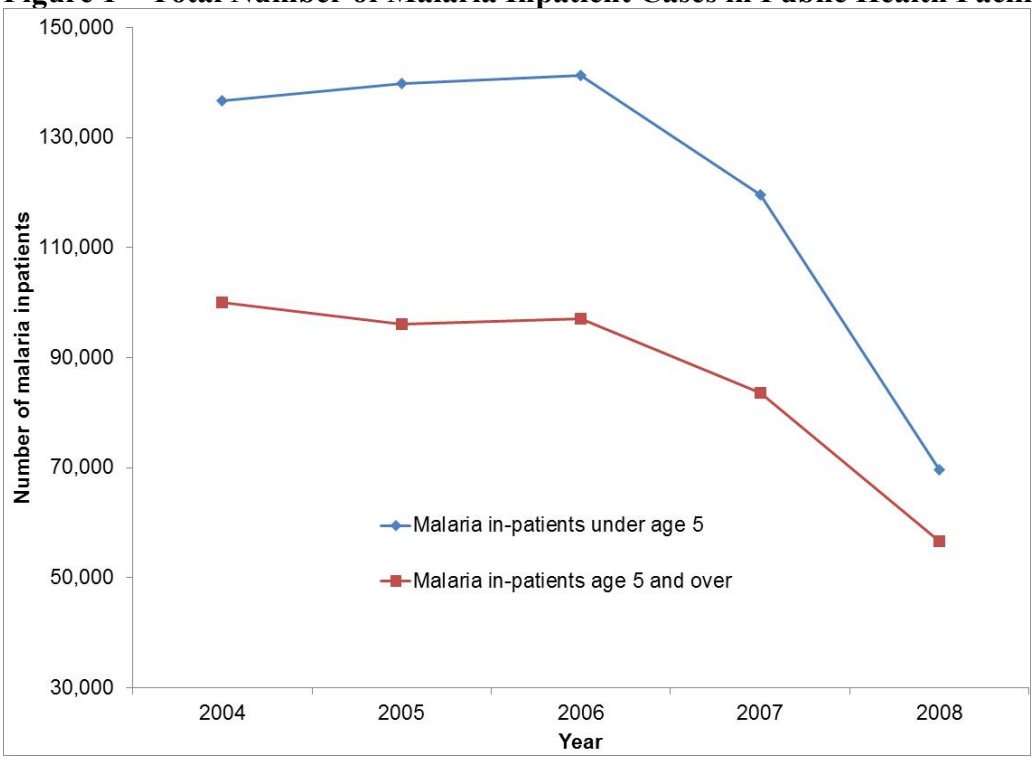
Table 7 – Rollback Malaria Exposure and Malaria Outcomes at Ages 3-5

	Positive Malaria Test	**Hemoglobin**	**Anemia**	**Severe Anemia**	**Fever and Anemia**
Post * MPP	0.157	-1.246*	0.301*	0.101**	0.336***
	(0.200)	(0.715)	(0.168)	(0.0490)	(0.115)
Observations	1,896	1,889	1,889	1,889	1,449
R-squared	0.322	0.185	0.149	0.063	0.163

Notes: Estimates of model (1) in main text, using biomarker data from the 2008 and 2010 Malaria Indicator Surveys. All models include controls for age and sex of child and district, survey year, cohort, province*survey year, province*cohort fixed effects. Robust standard errors, corrected for clustering at the district level, in parenthesis. Sample includes all children ages 3-5 who were born between 2004 and 2007. Post = 1 for the 2006 and 2007 birth cohorts, and 0 otherwise. MPP reflects the district specific under-5 malaria test positivity rate in 2006. *** p<0.01, ** p<0.05, * p<0.1.

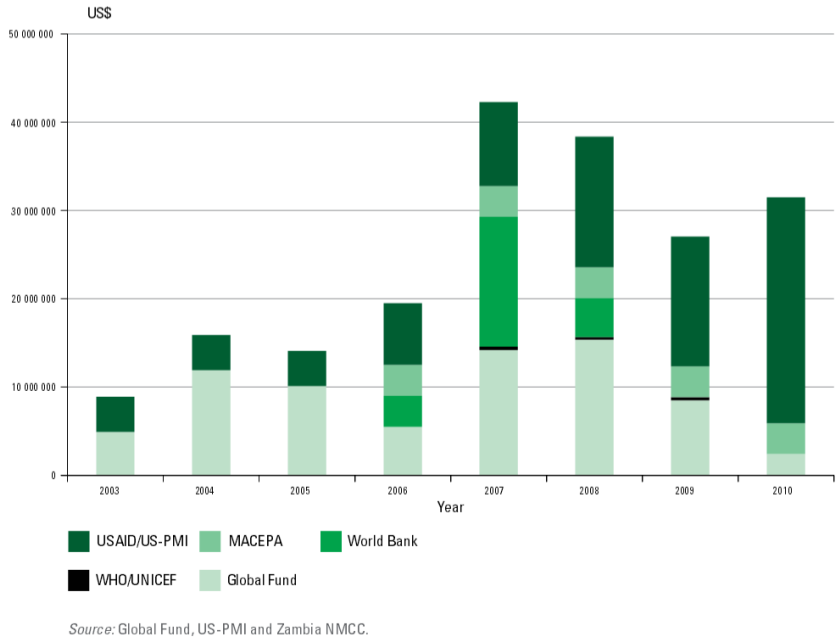
Appendix – Figures

Figure 1 – Total Number of Malaria Inpatient Cases in Public Health Facilities 2004-2008



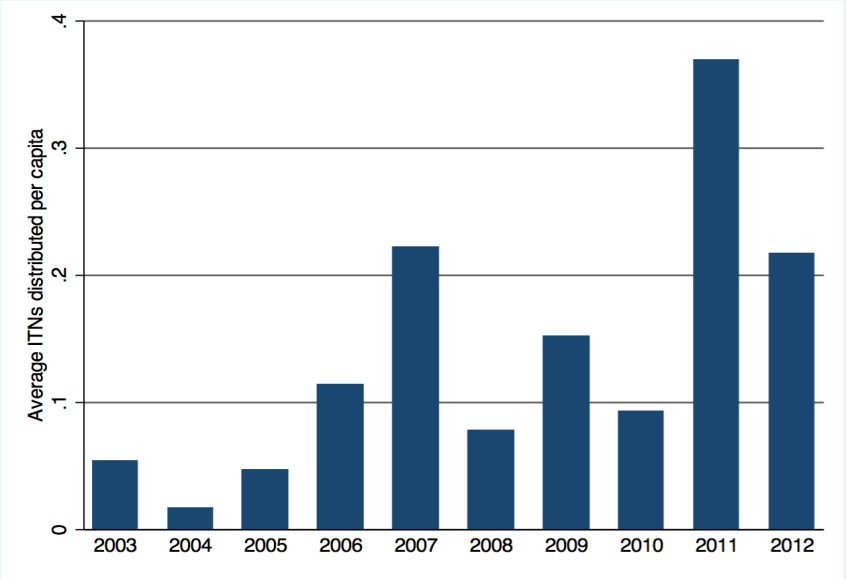
Notes: Data obtained from Zambia Health Management Information System, Ashraf et al. (2010), which was discontinued in 2009.

Figure 2 – Rollback Malaria Program Funding and Activity
A) Funding, 2003-2010



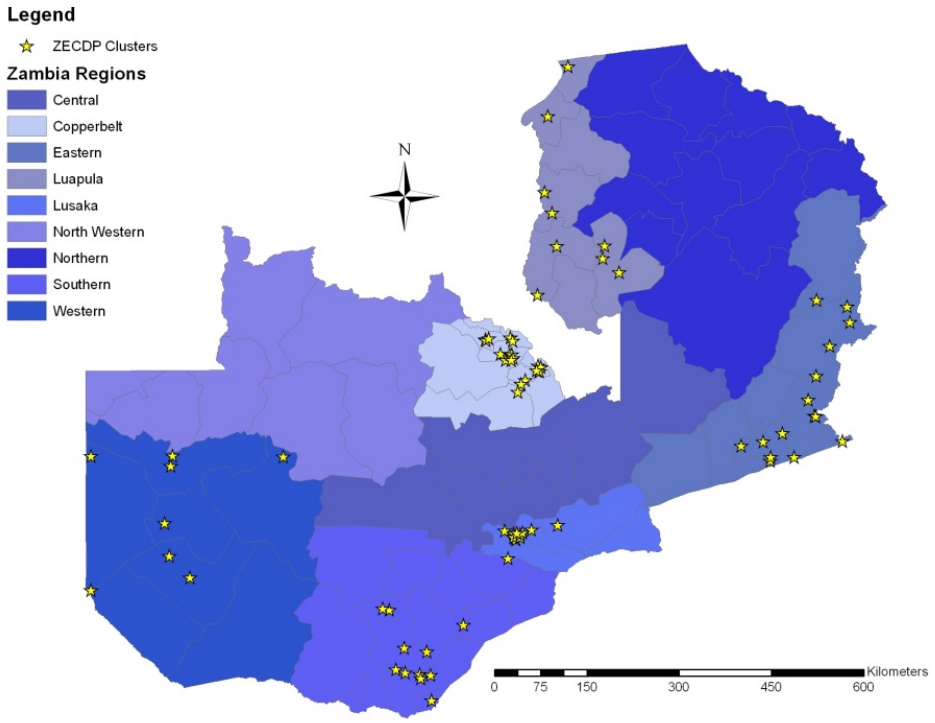
Source: Global Fund, US-PMI and Zambia NMCC.

B) Insecticide Treated Bed Net Distribution



Notes: Panel A shows external funding flows for malaria control efforts. The uptick in 2006 and spike in 2007 correlates with the initiation of the Rollback Malaria (RBM) program. The fall in funding in 2009 is timed with the corruption scandal discussed in the main text. That the funding shortfall was consequential is best seen in Panel B, where we plot the number of insecticide treated bed nets (ITN) distributed per capita in each year (data source: National Malaria Control Center Data Base). ITN disbursement followed 2 year cycles. The shortfall in ITN provision in 2009 (relative to 2007 and 2011) is coincident with the fall in program funding.

Figure 3 - Clusters sampled in the Zambia Early Childhood Development Project



Notes: A total of 73 clusters, denoted by yellow stars, were sampled as part of the ZECDP. Clusters in six of the nine Zambia provinces (Copperbelt, Eastern, Luapula, Lusaka, Southern, and Western) were sampled.

Appendix – Tables

Table 1 – Descriptive Statistics, ZECDP

	Obs	Mean	Std. Dev.	Min	Max
Developmental Outcomes					
Height-for-Age z-score	1952	-1.00	1.18	-5.43	5.46
Weight-for-Age z-score	1958	-0.86	1.01	-5.61	3.00
BMI-for-age z-score	1937	-0.30	0.94	-5.29	4.27
Physical Development Index	1937	0.00	1.00	-4.62	4.03
Peabody Picture Vocabulary z-score	2478	-0.01	1.01	-4.10	1.63
Expressive Language z-score	2348	-0.01	1.00	-1.76	1.42
Fine Motor z-score	2383	-0.02	1.01	-2.50	1.28
Kaufman Assessment Battery (K-ABC) z-score	2478	0.01	1.01	-0.95	4.60
Tactile Pattern z-score	2478	0.00	1.00	-1.78	2.22
NEPSY Block Test z-score	2478	0.00	1.00	-1.53	3.22
Rapid Naming Test z-score	2394	0.00	1.00	-6.65	1.53
Cognitive Development Index	2222	-0.01	0.99	-2.75	3.61
Attention (Pencil Tap Test) z-score	2463	0.01	1.00	-1.11	2.35
Child and Household Characteristics					
Female Gender (=1)	2656	0.48	0.50	0.00	1.00
Age (Months)	2711	73.61	3.48	67.00	84.00
Household Size	2676	6.05	2.30	2.00	18.00
Household Wealth Quintile	2711	2.91	1.40	1.00	5.00
Caregiver Schooling (Years)	2601	9.06	3.15	0.00	19.00
Household has Childrens' Books (=1)	2711	0.29	0.46	0.00	1.00
Adult Reads to Child (=1)	2711	0.48	0.50	0.00	1.00
Household has Other Books (=1)	2711	0.64	0.48	0.00	1.00
Cluster Level Measures					
Urban (=1)	53	0.49	0.50	0.00	1.00
*Cluster Malaria Parasite Prevalence, 2006 (*MPP)	*53*	*0.13*	*0.18*	*0.00*	*0.69*

Notes: Sample characteristics for ZECDP pooling both 2004 and 2006 birth cohorts. Developmental outcomes are described in detail in the main text and in Fink, et al (2012). "Physical Development Index" is the first principal component of the anthropometric z-scores. "Cognitive Development Index" is the first principal component of the Peabody Picture Vocabulary, Expressive Language, Fine Motor, K-ABC, Tactile Pattern, NEPSY, and Rapid Naming test z-scores. "Cluster Malaria Parasite Prevalence, 2006, or MPP) is the proportion of children in the 2006 Zambian Malaria Indicator Survey who tested positive for malaria by a rapid diagnostic test and slide based examination.

Table 2 – Descriptive Statistics, MIS

	Obs	Mean	Std. Dev.	Min	Max
Malaria/Health Outcomes					
Malaria Test Positive (=1)	5317	0.21	0.41	0	1
Hemoglobin (mg/dL)	5262	10.53	1.78	2	17.5
Anemia (=1)	5262	0.56	0.50	0	1
Severe Anemia (=1)	5262	0.04	0.20	0	1
Fever and Anemia (=1)	4135	0.23	0.42	0	1
Child Characteristics					
Age (Years)	6430	1.96	1.35	0	4
Female Gender (=1)	6430	0.49	0.50	0	1
Malaria Program Activities (Household)					
Household has ITN (=1)	6430	0.05	0.22	0	1
Household Received Insecticide Spray (=	6430	0.17	0.37	0	1
Number of Bed Nets in Household	6430	1.42	1.27	0	12
District Level					
Malaria Positivity Rate, 2006	5219	0.19	0.18	0	0.89

Notes: Sample characteristics for Malaria Indicator Survey (MIS), pooling 2006, 2008, and 2010 survey data and restricting the sample to the 2004-2007 birth cohorts. Malaria test positivity refers to rapid diagnostic test results. Anemia and severe anemia are based on hemoglobin thresholds of <11 and 7, respectively, following World Health Organization pediatric definitions. Fever and anemia refers to whether the child reported a fever in the last 2 weeks AND was anemic (hemoglobin < 11).

Table 3 – Descriptive Statistics, DHS

	DHS 2007			DHS 2013		
	Obs	Mean	Std. Dev.	Obs	Mean	Std. Dev.
Health Outcomes						
Fever in last 2 weeks	6401	0.162	0.368	13457	0.204	0.403
Child is stunted	5096	0.381	0.486	11373	0.337	0.473
Child is underweight	5096	0.190	0.393	11373	0.197	0.397
Child is wasted	5096	0.053	0.223	11374	0.055	0.229
Child has died	6401	0.087	0.282	13457	0.055	0.228
Child Characteristics						
Female Gender (=1)	6401	0.503	0.500	13457	0.493	0.500
Age in months	5621	27.695	17.063	12311	29.261	17.295
Year of birth	6401	2005	1.472	13457	2011	1.460
Maternal and household characteristics						
Mother education	6401	5.515	3.393	13442	6.049	3.623
Household has bed net	6401	0.712	0.453	13457	0.757	0.429
Household has electricity	6401	0.132	0.339	13457	0.179	0.383
Houshold has TV	6401	0.018	0.133	13457	0.051	0.219

Notes: All statistics represent unweighted sample average. Stunting, underweight and wasting are defined as HAZ, WAZ, and WHZ more than 2 standard deviations below the reference median.

Table 4 – Correlation Matrices, Child Development Indices

	MPP	Phys Index	Cogn Index	Attn. Z-Score
MPP	1.00			
Physical Development Index	-0.06	1.00		
Cognitive Development Index	-0.12	0.22	1.00	
Attention Z-Score	-0.08	0.12	0.50	1.00

Notes: Table displays the correlation between the key exposure measure, baseline (2006) under-5 malarial test positivity rates, on physical, cognitive, and non-cognitive outcomes. All variables as defined in the main text and listed in Appendix Table 2.

Table 5 – Rollback Malaria and Developmental Outcomes, Individual Tests

	Height-for-Age	Weight-for-Age	BMI-for-age	Peabody PV	Expressive Language	Fine Motor	K-ABC	Tactile Pattern	NEPSY Block Test
Post * MPP	0.213	0.15	-0.117	0.382	-0.564	0.342	-1.662***	-0.298	-1.456***
	(0.557)	(0.232)	(0.365)	(0.686)	(0.62)	(0.254)	(0.589)	(0.598)	(0.484)
Observations	1830	1835	1815	2322	2209	2242	2322	2322	2322
R-squared	0.25	0.198	0.154	0.394	0.312	0.257	0.362	0.324	0.373

Notes: Estimates of model (1) in main text for each developmental outcome. All models control for household wealth quintile, age and sex of child, caregiver education, and include cluster, cohort, and district*cohort fixed effects. Robust cluster corrected standard errors are in parenthesis. Estimates from Physical and Cognitive Development Indices derived from these measures are presented in *Table 2*. *** p<0.01, ** p<0.05, * p<0.1.

Table 6 – Falsification Check – Correlated Macroeconomic Shocks in DHS

	Stunted	**Underweight**	**Weight for height**	**Child death**
Post * MPP	-0.00675	0.0738	-0.229	-0.0185
	(0.0993)	(0.0641)	(0.223)	(0.0394)
Observations	4,021	4,021	4,022	4,709
R-squared	0.220	0.185	0.206	0.166

Notes: All models control cluster fixed effects, cohort fixed effects as well as region-specific time trends. Robust standard errors are clustered at the district level. Sample includes all children born in 2010 and 2012. Estimates are for model (1), but here we set Post=1 for cohort 2012 and 0 otherwise. The purpose of this model to assess whether shocks between 2010 and 2012, which is when the ZECDP was conducted, may be bias our core findings. MPP reflects the district specific under-5 malaria test positivity rate in 2006. Stunted and underweight are defined as HAZ, and WAZ < -2. Child death represents survival status at interview. *** p<0.01, ** p<0.05, * p<0.1.

Table 7 – Falsification Test, Changes in Rollback Malaria Inputs by Cohort

	ITN	Spray	Malaria Drugs
Post * MPP	0.0527	0.108	0.0946
	(0.0601)	(0.142)	(0.0805)
Observations	2,066	2,066	2,066
R-squared	0.160	0.243	0.085

Notes: Estimates of model (1) in main text, using malaria prevention and treatment item availability in the 2008 and 2010 MIS. All models control for age and sex of child, and include district, survey year, cohort, province*survey year, province*cohort fixed effects. Robust standard errors, corrected for clustering at the district level, in parenthesis. Sample includes all children ages 3-5 who were born between 2004 and 2007. Post = 1 for the 2006 and 2007 birth cohorts, and 0 otherwise. MPP reflects the district specific under-5 malaria test positivity rate in 2006. ITN = 1 if the household reported holding insecticide treated bednets, Spray = 1 if the household received indoor residual spraying, and malaria drugs = 1 if malaria episodes were treated with chemotherapy. *** $p<0.01$, ** $p<0.05$, * $p<0.1$.