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Caitlin E. Dunn

Approval Sheet

Retrospective Review of Onchocerciasis Control and Elimination Program Contributions to the Achievement of the Millennium Development Goals

By

Caitlin E. Dunn
Master of Public Health

Hubert Department of Global Health

_____

Deborah A. McFarland, PhD, MPH
Committee Chair

_____

Moses Katabarwa, PhD, MPH
Committee Member

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By

Caitlin E. Dunn
B.A., Pepperdine University, 2006

Thesis Committee Chair: Deborah A. McFarland, PhD, MPH

An abstract of
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Abstract

Retrospective Review of Onchocerciasis Control and Elimination Program Contributions to the Achievement of the Millennium Development Goals

By Caitlin E. Dunn

In 2000, 189 member states of the United Nations (UN) developed a plan for peace and development, which resulted in eight actionable goals known as the Millennium Development Goals (MDGs). Since their inception, the MDGs have been considered the international standard for measuring development progress and have provided a blueprint for global health policy and programming. However, emphasis upon the achievement of priority benchmarks around the 'big three' diseases - namely HIV, TB and malaria - has influenced global health entities to disproportionately allocate resources. Meanwhile, several tropical diseases that almost exclusively impact the poorest of the poor continue to be neglected, despite the existence of cost-effective and feasible methods of control and elimination.

One of these Neglected Tropical Diseases (NTDs), onchocerciasis, commonly known as river blindness, is a debilitating and stigmatizing disease primarily affecting individuals living in remote and impoverished areas. Programs to control onchocerciasis are considered to be some of the most successful and cost-effective public health campaigns ever launched. In addition to improving the health and well-being of millions of individuals, these programs also lead to improvements in education, agricultural production, and economic development in affected communities. This paper reviews the contributions that such concentrated efforts to control and eliminate onchocerciasis make to achieving select MDGs. The author hopes to draw the attention of public policymakers and global health funders to the role onchocerciasis and other NTDs play in hindering development and advocate for their inclusion in the post 2015 agenda.

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And finally, I would like to dedicate this thesis to the individuals and communities who are working to bring an end to this debilitating disease: May your tenacity continue to serve as an inspiration to me throughout my public health career.

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Abbreviations

APOC	African Program for Onchocerciasis Control
CDD	Community-Directed Distributor
CDTI	Community-Directed Treatment with Ivermectin
DALY	Disability Adjusted Life Year
DOTS	Directly Observed Treatment, short course
EPI	Expanded Program on Immunization
ERR	Economic rate of return
FAO	Food and Agriculture Organization
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
LF	Lymphatic Filariasis
LLIN	Long Lasting Impregnated Nets
MDA	Mass Drug Administration
MDGs	Millennium Development Goals
MDP	Mectizan Donation Program
Mf	Microfilariae
NGDO	Non-Governmental Development Organization
NTDs	Neglected Tropical Diseases
OCP	Onchocerciasis Control Program in West Africa
OEPA	Onchocerciasis Elimination Program for the Americas
OSD	Onchocercal Skin Disease
PLoS	Public Library of Science
R&D	Research and Development
REMO	Rapid Epidemiological Mapping on Onchocerciasis
STH	Soil-Transmitted Helminthiases
TB	Tuberculosis
TDR	WHO-based Special Program for Research and Training in Tropical Diseases
UN	United Nations
WHO	World Health Organization

CHAPTER I: INTRODUCTION

Significance of the Project

This thesis addresses the contributions of onchocerciasis control and elimination programs towards achieving several of the targets set forth in the Millennium Development Goals (MDGs). Onchocerciasis, more commonly known as river blindness, is a debilitating and stigmatizing disease, predominantly affecting individuals living in remote and impoverished areas – the primary population which the MDGs are intended to help. Onchocerciasis control is considered to be one of the most successful and cost-effective public health campaigns ever launched. The programs' successes reach beyond the improved health and wellbeing of millions of individuals, leading to improvements in education, agriculture production and the economic development of affected communities [1,2].

Since their inception in 2000, the MDGs have provided a blueprint for global health policy and programming as they draw attention to the central link between poor health and poverty. Although data limitations have led to some concerns over their utility in gauging the equity and sustainability of achievements [3-5], the MDGs are considered to be the international standard for measuring progress in development as they allow for national comparisons and hold governments accountable to time-bound and specific targets [6].

While a plethora of information on onchocerciasis exists, research reveals few articles that point specifically to these programs being used as a strategy to achieve the MDG targets. Furthermore, despite the recognition of the detrimental effect of onchocerciasis and other Neglected Tropical Diseases (NTDs) on development, and the documented success of control and elimination programs, they were not prioritized in the MDG agenda. Instead, NTDs fall into the bundled category of "other diseases" in MDG six [1].

Rationale For Article And Targeting Journal

The purpose of this thesis is threefold: 1) to draw the attention of public policy makers and global health funders to the role NTDs play in hindering development and advocate for the inclusion of NTDs in the post 2015 agenda; 2) to show how focusing on a data-driven program leads to progress towards certain MDGs and; 3) to highlight the achievements of The Carter Center and its partners in combating onchocerciasis.

A condensed manuscript version of this thesis will be submitted to the Public Library of Science (PLoS) NTDs once the supporting authors provide final comments and approval. The PLoS NTD journal was chosen as an appropriate outlet based on its readership and reputation. As one of the leading open access peer reviewed journals of tropical medicine, it is hoped that this article will reach a broad community. This paper will be the last of three articles that were commissioned by The Carter Center's Health Programs to highlight the contributions of NTD control and elimination. The first, which focuses on Guinea Worm, was published in PLoS NTD in May 2013 and the second, on Trachoma, has been submitted and is awaiting acceptance. The journal allows for 3,000 words and several tables and figures.

Background

Millennium Development Goals

In 2000, 189 member states of the United Nations (UN) came together, in what was then the largest gathering of world leaders, for a three-day summit resulting in the adoption of the United Nations Millennium Declaration. In signing this declaration, the global community committed to uphold the dignity, equality and human rights of all people while working together for peace and development. Eight goals were set to reduce extreme poverty and ensure the rights of all people to education, gender equity, health, and environmental sustainability (Table 1). In

order to reach these goals by 2015 and measure progress, 18 time-bound targets and 48 indicators were developed using data from 1990 as a baseline [6,7]. (See Appendix for full listing of MDGs, targets and indicators)

The MDGs are useful for many reasons including holding governments accountable. Annual progress reports, published by the Statistics Division of the UN Department of Economic and Social Affairs, measure change over time and compare countries' progress toward each goal. Included in these reports are model trajectories that illustrate which targets countries are on track to meet, and in which areas they are lagging behind. This visual presentation of data is useful to government officials so they can make sure policies and budgets line up with priority development areas. The role developed countries play in reaching these goals is emphasized by including targets for international assistance and debt relief, fair trade, partnerships and access to medicine and technologies [6].

The MDGs have also brought greater attention to the relationship between poor health and poverty [8]. Considering "three of the eight goals, eight of the 18 targets and 18 of the 48 indicators relate to health," there is no way that the MDGs can be accomplished without focusing on improving health [6,9]. Consequently, the MDGs have provided a blueprint for global health policy and programming for the past decade.

While there are geographic variations in levels of success for each MDG, the overall direction has been positive. Compared to 1990, half as many people live in extreme poverty and the proportion of people without access to improved water sources has been halved. There have also been significant improvements in health. For example, mortality rates for malaria fell by 25% between 2000 and 2010, and treating people for tuberculosis has saved approximately 20 million lives [10].

Nevertheless, there are some limitations to using the MDGs as the standard of development progress. First and foremost, the MDGs are national indicators, so they do not reveal distributional inequality in gains, such as those between wealth quintiles or across the rural-urban divide. The use of aggregate data can mask disparities since a goal can be achieved even if gains were attained in one region, or by one group of people, who were not necessarily the most at-need [6]. It is also difficult to measure progress because the baseline data are incomplete, national data management systems vary in quality, and the indicators are not always comparable between countries. Some scholars have suggested that there may be some unintended consequences as well. For instance, by focusing on quantifiable indicators, such as total primary school enrollment, the quality of education services may be undermined [5]. Similarly, emphasis upon achievement of priority benchmarks may have influenced global health entities to disproportionately allocate resources and attention on the 'big three' - namely HIV, TB and malaria – and neglect other diseases, which cause comparable disability and suffering in vulnerable populations.

Table 1: Millennium Development Goals and Targets

Millennium Development Goals and Targets	
Goal 1: Eradicate extreme poverty and hunger	Target 1.A: Halve, between 1990 and 2015, the proportion of people whose income is less than one dollar a day
	Target 1.B: Achieve full and productive employment and decent work for all, including women and young people
	Target 1.C: Halve, between 1990 and 2015, the proportion of people who suffer from hunger
Goal 2: Achieve universal primary education	Target 2.A: Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary schooling
Goal 3: Promote gender equality and empower women	Target 3.A. Eliminate gender disparity in primary and secondary education, preferably by 2005, and in all levels of education no later than 2015
Goal 4: Reduce child mortality	Target 4.A: Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate
Goal 5: Improve Maternal Health	Target 5.A: Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio
	Target 5.B: Achieve, by 2015, universal access to reproductive health
Goal 6: Combat HIV, AIDS, malaria and other diseases	Target 6.A: Have halted by 2015 and begun to reverse the spread of HIV/AIDS
	6.B: Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it
	6.C: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases
Goal 7: Ensure environmental sustainability	Target 7.A: Integrate the principles of sustainable development into country policies and programs and reverse the loss of environmental resources
	Target 7.B: Reduce biodiversity loss, achieving, by 2010, a significant reduction in the rate of loss
	Target 7.C: Halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation
	Target 7.D: By 2020, to have achieved a significant improvement in the lives of at least 100 million slum dwellers
Goal 8: Develop a global partnership for development	Target 8.A: Develop further an open, rule-based, predictable, non-discriminatory trading and financial system
	Target 8.B: Address the special needs of the least developed countries
	Target 8.C: Address the special needs of landlocked developing countries and small island developing States
	Target 8.D: Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term
	Target 8.E: In cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries
	Target 8.F: In cooperation with the private sector, make available the benefits of technologies, especially information and communications

Neglected Tropical Diseases

Neglected Tropical Diseases (NTDs) are a group of parasitic and bacterial infections that are classified together because of their geographic affinity, historically low research priority, and the negative impact they have on the health and economic prospects of the populations they affect. NTDs are some of the oldest afflictions known to humankind, with descriptions of the suffering caused by them found in the Bible, the Talmud and writings of Hippocrates [11]. It is estimated that over one billion people, or approximately a sixth of the world's population, are infected with one or more NTDs, and they are among the most common infectious diseases affecting the poor [12].

The "bottom billion," or estimated 2.7 billion people who live on less than two dollars a day, often lack basic necessities such as safe water, sanitation, and adequate shelter, are malnourished and lack access to health facilities [11-13]. These conditions, paired with tropical and sub-tropical climates that allow protozoa, bacteria and helminthes to thrive, make these populations more vulnerable to infection. In fact, 70% of the countries where NTDs are endemic are low-income or lower middle-income, and all low-income countries are affected by at least 5 NTDs. Since NTDs often overlap geographically, it is not unusual for individuals to be polyparasitized [12]. Conflicts and government instability tend to exacerbate NTD infection as people are forced to migrate and there are few health services available [14].

Collectively, NTDs cause a disability burden equivalent to one quarter that of HIV and almost equal to that of malaria [8], yet the attention paid to NTDs is not commensurate. A glance at the allocation of funds by global health entities illustrates this disparity; while HIV/AIDS programs received 37% of total international development

assistance in 2010, NTDs received a mere 0.6% [15]. Part of the rationale for the current disease prioritization is that NTDs are not major causes of mortality. However, given that these diseases lead to the disability, disfigurement, stigmatization and suffering of millions [11,13], measures of quality of life should receive greater consideration.

Another factor that contributes to the neglect of these diseases is that they primarily affect marginalized populations, who lack political voice, and are tied to certain geographical zones, where they pose no threat to wealthier populations [11]. A 2012 report from the World Health Organization's (WHO) Special Program for Research and Training in Tropical Diseases (TDR) indicated that research into diseases that affect the poor is considerably less than research into diseases of the wealthy [16]. This gap exists, in large part, because there is little incentive for pharmaceutical companies to invest in research and development (R&D) of drugs and vaccines for which there is no market. Again, the numbers paint an accurate picture; out of the 1,233 drugs approved for human usage between 1975 and 1997, only 4 are effective in treating NTDs [11]. Even ivermectin, which is now used to treat river blindness, was originally developed to treat parasites in livestock as there was a large veterinary market for anthelmintic drugs [11,17].

Despite these challenges, the fight against NTDs has come a long way. One of the most significant advancements in NTD control has come about thanks to the generous drug donations of several pharmaceutical companies. Through public-private partnerships in which drugs are made available for free, or at reduced cost, Mass Drug Administration (MDA) now offers relief from many of these ancient afflictions. With the establishment of Product Development Private-Public Partnerships, there are more incentives to focus

on developing products for resource poor countries. In addition, some developing nations, which experience endemic NTDs, are now beginning to invest in their own R&D [1,11].

In recent years, the global health community has shown more interest in NTDs and the opportunity integrated drug delivery offers to combat multiple diseases simultaneously. Most notably, in January of 2012, ministries of health of endemic countries, leading global health agencies, pharmaceutical companies, donor agencies and members of the scientific community came together to sign the London Declaration on Neglected Tropical Diseases. In endorsing this declaration, the partners committed their resources to sustain and expand NTD programs. Specifically, the document outlines targets for 10 NTDs by 2020: the control of schistosomasis, Chagas disease, visceral leishmaniasis, soil transmitted helminths (STHs), and onchocerciasis; the elimination of lymphatic filariasis, leprosy, trypanosomiasis and blinding trachoma; and the eradication of guinea worm [18]. These NTDs were selected because they cause the greatest disease burden and/or can be controlled with existing strategies [14]. With cost-effective and practical solutions at hand, NTD control and elimination is a sound investment in health and, furthermore, a way to uphold the dignity, equality and human rights of all people as was called for in the Millennium Declaration [7,19,20].

Onchocerciasis

Onchocerciasis, commonly known as river blindness, is one of the most common and costly NTDs. Endemic to 31 African countries as well as 6 countries in the Americas and several foci in Yemen, over 100 million people are at high risk of infection worldwide [21]. Of the estimated 37 million people currently infected, 99% live in sub-Saharan Africa [22,23]. Nigeria, alone, accounts for nearly a quarter of infections [2]

Figure 1: Lifecycle of Onchocerca Volvulus

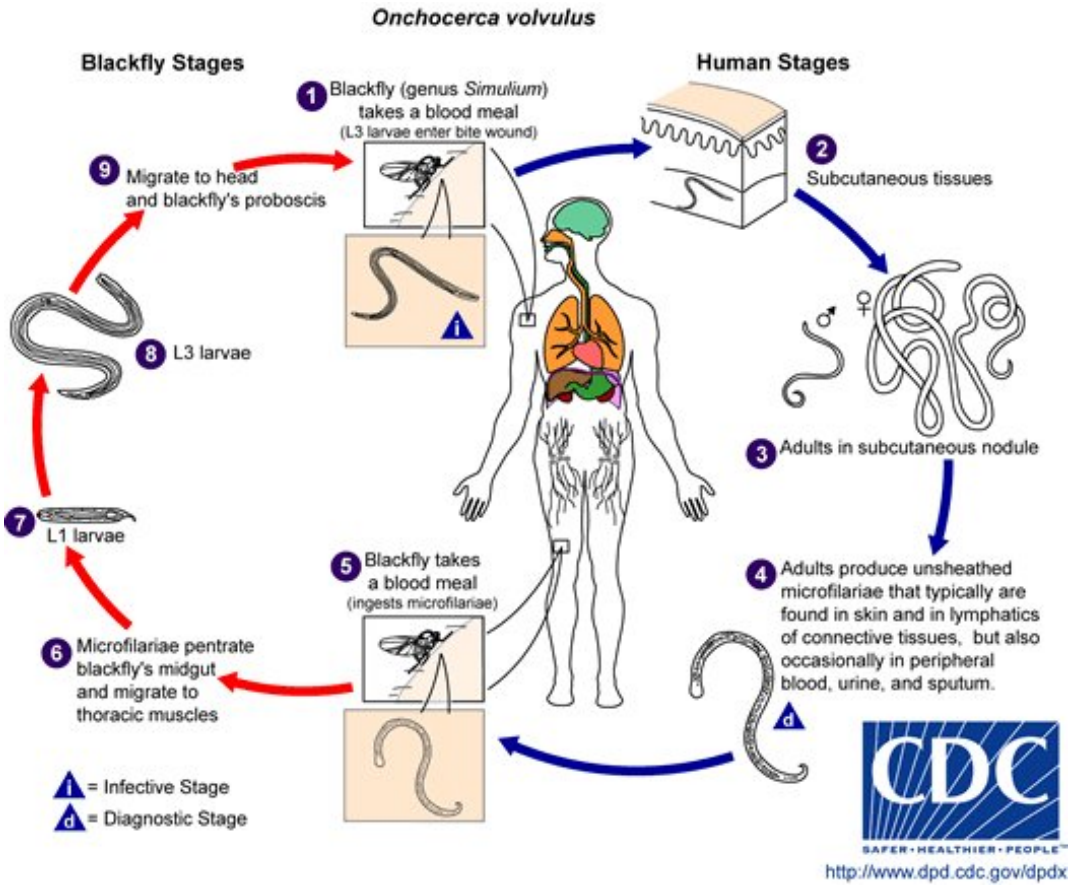


Image from Center for Disease Control

The Parasite

Onchocerciasis is caused by infection with the parasitic nematode worm, Onchocerca Volvulus, transmitted by black flies of the genus Simulium. An individual becomes infected when a fly bites and deposits one or more O. Volvulus larvae into their bloodstream [24]. Larvae develop into adult worms in the course of about one year; females can grow to about a meter in length and 0.25-0.45 mm in diameter, while the males are usually only about 2-5 cm in length and 0.1-0.2mm in diameter [22,25]. The adult worms often congregate and hide out in “coiled mating pairs” inside fibrous

nodules that develop in subcutaneous tissue. After mating with a male worm, the female begins releasing thousands of embryos, called microfilariae (mf), per day [22,26]. These microscopic larvae migrate throughout the body, in the intercellular fluid of the dermis, in order to make themselves available to the black fly [27]. Once taken up in a blood meal, the mf develop into infective larvae (L3) inside the gut of the black fly, and then move to its head and proboscis where they can then be deposited into a human host, completing their lifecycle [23].

The adult worms lives an average of 12-15 years with a reproductive lifespan of 9-11 years [25]. Mf can live between 6 months and two years if they are not taken up by a black fly [28]. When they die, they invoke an inflammatory immune response in their human host, causing intense itching [27]. In 2002, it was determined that the endosymbiotic bacteria, Wolbachia, which is released following the death of mf, may be the true cause of the inflammatory response [2]. Whatever the source, this repeated reaction can destroy tissue and cause damage to the eyes, skin and possibly the brain [26]. If treated early enough, much of the damage can be reversed, but chronic infection can lead to permanent blindness and skin disease [26].

The Vector

Black Flies are an intermediate host of the parasite and are needed to complete the lifecycle [22]. There are more than 700 Simulium species, but only a handful transmit Onchocerca Volvulus [25]. These species have many nuanced differences in terms of their behavioral habits and efficiency as vectors, but for operational purposes, they are generalized into two groups: based on their habitat proclivity, they are referred to as the "forest form" and the "savanna form." One of the main differences between these vectors

is related to how the disease is manifested in humans. The savanna form causes at least three times more blindness than the forest form, even when controlling for microfilarial load, while the forest form causes more severe skin disease [29].

Level of infection is related to frequency of exposure and the efficiency of the vector [25]. In the most endemic regions, people may be bitten up to 10,000 times a day [17]. Typically, those who live or work closer to breeding sites have more exposure to the fly, which is why farmers and fishermen often have higher levels of infection [25].

The black fly tends to be found in the most fertile of environments [2]. All species breed in fast flowing highly oxygenated waters, where they typically lay their eggs on underwater vegetation. The forest forms have the added niche of traveling on freshwater crabs, prawns and nymphs of mayflies, making vector control, in certain foci, more feasible. For the most part, the black fly stays near the river, having a flight range of about 12 km, but in the Western Savannah the flies have been known to ride along the winds, reaching as far as 600km [22,27,30].

Associated Morbidities

Onchocerciasis is the second leading infectious cause of preventable blindness [1]; as of 2006, it was estimated that 1.5 million people have severe visual impairment and 600,000 are blind are a result of infection [17]. Damage to the anterior segment of the eye is thought to result from post-death inflammatory response, whereas damage to the posterior segment, which causes optic nerve damage, is now thought to stem from an autoimmune response. This is significant because it means retinal lesions may progress even after the parasite is cleared – a finding that resulted from the discovery of an

association with past microfilarial load and blindness in retrospective studies of the Onchocerciasis Control Program (OCP) cohort [23].

While blindness may be the most serious consequence of onchocerciasis, those affected report that itching and changed physical appearance are the most burdensome symptoms [27]. The itching can be so severe as to cause insomnia, and individuals, so desperate to find some relief, have been known to break clay pots and heat irons to scratch themselves [31]. Others have considered and even been driven to suicide [32,33]. Moreover, people often develop papular rashes which, when scratched, open up and bleed, providing entry for secondary infections [27].

Telltale signs of onchocerciasis include spots of depigmentation, commonly referred to as "leopard skin," rough, wrinkled skin known as "lizard skin," and nodules (hosting the adult worms) that can often be seen and felt on the body. Additionally, infected people can experience poor nutritional status, fatigue, musculo-skeletal pain, headaches and elephantiasis of the genitals [23,27,29]. With chronic infection, the skin becomes fragile, atrophied, and inelastic. When this happens in the genitals, it can result in so-called "hanging groin" [25,34]. This in turn affects the sexual life of those infected, as those with genital distortion may have problems performing and fear embarrassment [27,35]. Severity and reaction to the infection varies greatly in individuals suggesting a complex host-parasite interaction, possibly related to immune response [29].

Microfilariae have been found in the organs, bodily fluids, and tissues of people living in endemic areas but the full effects on the body, aside from eye and skin disease, are not known. In particular, researchers are looking into the effect of microfilariae on the brain, as there appears to be a relationship between high microfilarial load and certain

types of epilepsy [23,26,36]. In parts of Uganda, locals associate onchocerciasis with other illnesses including Nakalanga Syndrome (dwarfism) and a type of epilepsy known as Nodding Syndrome [2]. The association between onchocerciasis and epilepsy has been suspected in Africa as well as parts of Latin America. Case control studies in Cameroon and Burundi found that people with onchocerciasis infection have higher incidence of epilepsy, but the findings are still debated as there may be other factors confounding the relationship [37]. Studies in Ecuador, Tanzania, Mali, and Nigeria found that locals believe onchocerciasis causes reproductive problems including spontaneous abortion, stillbirth and infertility [29,38]. While not substantiated with evidence, these beliefs still have bearing as people infected are avoided because of cultural beliefs as to disease transmission [39].

It is now estimated that there are 1.5 million Disability Adjusted Life Years (DALYS) lost annually due to onchocerciasis [1]. (See appendix for more information on DALYs). While visual loss was originally thought to account for the majority of the disease burden, in recent years, the true degree of disability caused from Onchocercal Skin Disease (OSD) has been brought to light. Severe itching now accounts for 60% of disease burden and blindness/ loss of visual acuity represents the other 40% [39]. Even now, the burden of onchocerciasis may be underestimated; since the number used to calculate the burden of onchocerciasis is gathered from treatment data, and only communities living in mesoendemic and hyperendmic regions[1] were treated historically, the true number of people suffering from onchocerciasis is not known [13].

[1] Meso endemic corresponds to an infection prevalence of 40%-59% and hyper endemic corresponds to prevalence greater than 59% of the population

Aside from the physical manifestations of the disease, there are major social and economic impacts. Infected individuals often have poor mental health as they are ostracized from their communities [13,35,40,41]. Women, in particular, suffer from stigma as OSD affects their marital prospects and, thus, economic security [29]. The disability caused by onchocerciasis greatly reduces productivity in the home, work, and school, all of which adversely affect development. These secondary effects will be discussed in greater detail in the results section.

Treatment

Onchocerciasis is primarily controlled through Mass Drug Administration (MDA) of ivermectin (brand name Mectizan®). Ivermectin is a safe and effective antehelminth drug that works by killing microfilaria and reducing the reproduction rate of the adult worm. One dose, administered annually, can kill up to 95% of larvae and bring relief from most of the morbidities associated with onchocerciasis [17,22]. In most affected countries in Africa, control programs (see Table 2) aim for 65% therapeutic coverage of meso and hyper endemic communities once per year; a strategy that has proven to be an effective control mechanism [28].

Table 2: Control Versus Elimination

Control Versus Elimination Program Goals[2]
Control: "The reduction of incidence or disease manifestations to a predefined point at which public health authorities declare the condition to no longer be a public health problem. Continued measures are needed to keep transmission or morbidity at or below this point."
Elimination: "A reduction to zero of the incidence of infection caused by a specific agent in a defined geographic area as a result of deliberate interventions efforts; continued measures to prevent reestablishment of transmission are required."

Though control has been a major public health achievement, mathematical models suggest it is possible to eliminate onchocerciasis where transmission can be interrupted long enough for the parasite to die out in its human reservoir [24]. Ivermectin temporarily suppresses transmission by lessening the chance the microfilaria will be taken up by a black fly, but after a few months, females can begin producing at a level high enough to continue the transmission cycle. Without the discovery of an effective macrofilaricide,[3] it was thought treatment with ivermectin would need to be continued throughout the worm's 10- 15 year lifespan [22]. Fortunately, operational research has shown that semi-annual treatment with ivermectin has a significant impact on the adult worm; thus, if programs increase treatment frequency, the timeframe necessary for elimination can be shortened significantly [42]. In the Americas, where regional elimination is the end goal, countries have seen positive results using this strategy of semi-annual MDA. Transmission of O. Volvulus has been interrupted in Mexico, Ecuador, and Guatemala,

[2] Definitions were taken from the Final Report of the Conference on the Eradicability of Onchocerciasis; The Carter Center, 2012

[3] Macrofilaricides are effective at killing adult worms, whereas microfilaricides only kill larvae

with treatments only remaining necessary deep in the Amazon, on the border of Brazil and Venezuela [43].

In light of these and other successes, the African Program for Onchocerciasis Control (APOC) announced is will be transitioning to a goal of elimination in 2016 [44]. This change in mandate will necessitate new strategies, such as starting treatment in hypo endemic regions and increasing treatment frequency and coverage.[4] Perhaps of equal importance, it will require the renewed commitment and tenacity of all involved, as Africa's expansive terrain produces unique challenges, including regions co-endemic for loaisis (Loa Loa), and areas ridden with conflict. Loa Loa is filarial disease endemic to Cameroon, the Central African Republic, the Congo, Democratic Republic of the Congo, Nigeria and South Sudan; its presence limits the expansion of MDA as ivermectin can cause encephalopathy in individuals who are co-infected [23,44].

History of Control & Elimination Programs

When initial epidemiological research into the extent of onchocerciasis in West Africa was conducted in the 1970s, the socio-economic consequences of the disease were revealed to be devastating. Over 60 percent of the savannah population was infected, with 10% of the adult population blind and 30% visually impaired. Moreover, half of the men over the age of 40 were blind and the disease was already affecting children [22]. It has been estimated that 2 million individuals in West Africa were infected with onchocerciasis and 200,000 were blind [17]. In an attempt to escape this scourge, entire villages would move away from the fertile river valleys that were home to the black fly. Living in over-crowed villages with poor soil and less access to water, agriculture yields

[4] Elimination programs must reach a therapeutic coverage level of 80% in all endemic communities to interrupt transmission. (WHO Certification of the Elimination of Onchocerciasis Guidelines, 2000)

were reduced, and subsequently families suffered from hunger and were pushed further into poverty [22].

Launched in 1974, the Onchocerciasis Control Program (OCP), a joint effort of the World Bank, the Food and Agriculture Organization (FAO), the United Nations (UN) and World Health Organization (WHO), was mandated to "eliminate river blindness as a public health problem and as an obstacle to socioeconomic development" [22]. Primarily a vector control program, helicopters were used to spray larvicides over breeding sites in the Volta River Basin Area on a weekly basis. Originally covering Benin, Burkina Faso, Cote d'Ivoire, Ghana, Mali, Niger and Togo, the program expanded to Guinea, Guinea-Bissau, Senegal and Sierra Leone when it was discovered the black fly was reinvading the control area. In some areas, insecticide resistance was emerging, however, the OCP managed to stay ahead of the problem by developing alternative drugs, which they used in rotation [22].

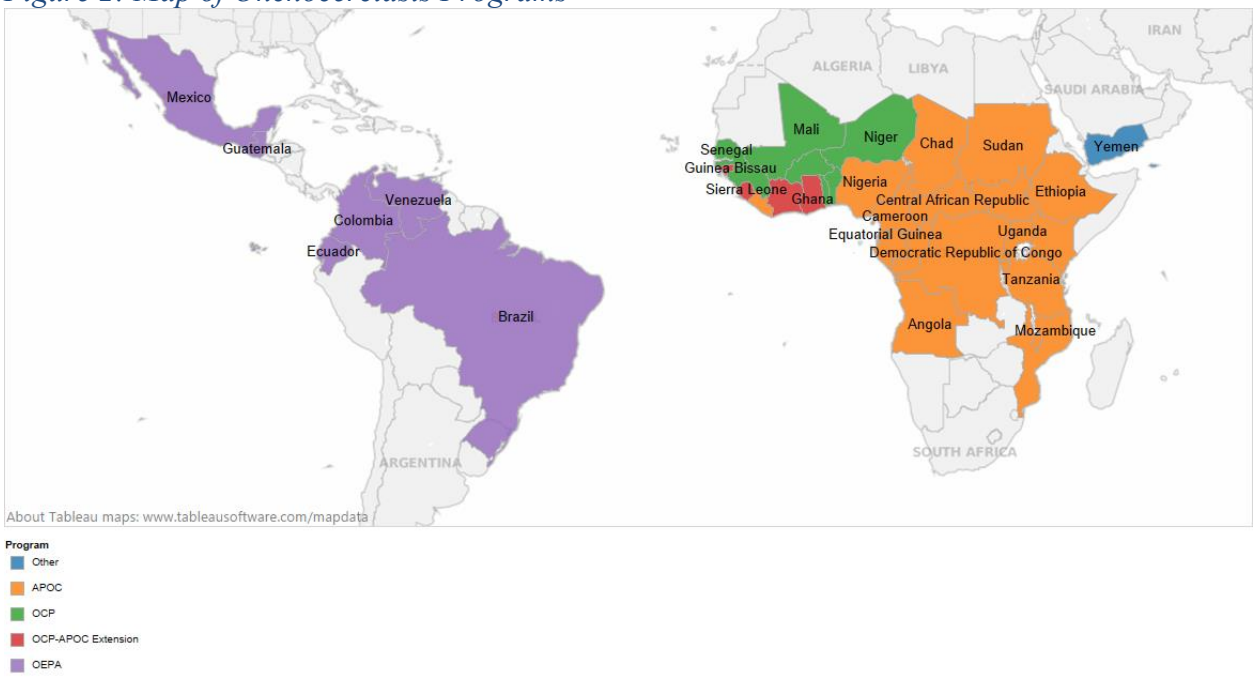
When ivermectin was discovered to be a safe and effective drug in humans, OCP conducted some of the first field trials and found it to be a useful supplementary control tool [22]. While larviciding controlled the vector, successfully reducing transmission rates, it did not help those already infected; the addition of ivermectin brought relief to those already suffering from the disease [45]. In 1990, OCP began sending mobile teams to deliver the drug to "extension areas." Local health staff would gather communities in a central location so the drug could be administered during one campaign. However, this was prohibitively costly, and was determined to be ineffective since large parts of the villages would miss the clinic, making it impossible to reach the necessary coverage levels. When the drug was determined to be safe enough to be administered without

supervision, the teams began leaving drugs to be administered to people who had been absent. This strategy was the predecessor to community-directed distribution [22].

At the end of program in 2002, onchocerciasis transmission was halted in all but three OCP countries, and was eliminated as a disease of public health importance from 10 of the 11 OCP countries [2]. Programs in Sierra Leone were hindered due to ongoing conflict [45].

Established by the Ministries of Health of the affected countries, with support from The River Blindness Foundation, the Onchocerciasis Elimination Program of the Americas (OEPA) was launched in 1992. The goal of OEPA is to interrupt disease transmission and eliminate morbidity from onchocerciasis in the 13 endemic foci in South and Central America [2,46,47]. The strategy implemented is twice yearly treatment with ivermectin for those living in endemic regions, with the minimum treatment goal of 85% of those at risk [2]. Since its implementation, onchocerciasis has been eliminated in Colombia and transmission has been interrupted in Ecuador, Mexico and Guatemala. Currently, ivermectin is only being distributed in Brazil and Venezuela [2]. (See Figure 2).

Figure 2: Map of Onchocerciasis Programs



The African Program for Onchocerciasis Control (APOC) started in 1995 with goal of eliminating onchocerciasis as a public health problem in the 19 endemic African countries that were not a part of the OCP[2].[5] The WHO oversees the program with financial backing from a trust fund managed by the World Bank and support from an extensive partnership, including affected governments and communities, multilateral organizations, non-governmental development organizations (NDGOs), donor agencies, researchers and private sector companies [48]. Due to cost and ecological differences, aerial spraying used in OCP areas was not deemed a feasible option in APOC areas. Instead, APOC has developed an extensive network of Community Directed Distributors (CDDs) to facilitate MDA within their communities. This strategy of Community Directed Treatment with Ivermectin (CDTI) allows communities considerable agency in

[5] Four of the original OCP countries now receive ivermectin treatments through APOC as there were concerns over recrudescence

drug delivery, deciding when and how drug treatment will occur [48]. The program was designed in two phases: The first focused on developing a sustainable delivery system, and the second set as a "phasing out" period in which endemic countries would transition into full management of their programs [2,48]. While APOC was originally supposed to end by 2010, it was extended to 2015 and then 2025, as they considered moving from control to elimination [2,39].

Program Partners

The partnership forged to fight onchocerciasis has spanned multiple continents and decades, led to innovations and best practices in the field of disease control, and opened doors for further collaboration and integration [49].

The APOC, which is the coordinating agency for onchocerciasis programs in Africa, is housed and managed at the WHO with financial management from The World Bank. The partnership includes the active involvement of over 190,000 communities and 19 Ministries of Health in affected countries, donor countries and UN agencies, private foundations, researchers, pharmaceutical companies, and a host of local and international Non-Governmental Development Organization (NGDOs). These NGDOs include: Christoffel Blindemmission, Helen Keller International, Interchurch Medical Assistance World Health, Light for the World, Lions Club International Foundation, Mission to Save the Helpless, Organisation pour la Prévention de la Cécité, Sight Savers International, United Front Against River Blindness and The Carter Center. [44]

In the Americas, Onchocerciasis elimination programs are coordinated by the OEPA, which is currently led and supported by The Carter Center. The partnership

includes the Ministries of Health in the six affected countries, and financial and technical support of the Pan American Health Organization, the Bill and Melinda Gates Foundation, the US Centers for Disease Control and Prevention, and the Lions Club International Foundation. [50]

CHAPTER II: LITERATURE REVIEW

Millennium Development Goals (1-8)

MDG 1: Eradicate extreme poverty and hunger

A literature review revealed that onchocerciasis infection exacerbates poverty through three main avenues: decreasing worker productivity and earnings, reducing potential agricultural yields and increasing medical expenses. Studies looking at the economic impact of onchocerciasis include cost-benefit analyses, calculations of direct and indirect costs of individuals and communities, and cost effectiveness analyses that often use a measurement of disease burden such as DALYs [51]. (see Table 3).

Table 3: Types of Economic Analyses

TYPES OF ECONOMIC ANALYSES FOR HEALTH [51]	
Cost Calculations	Calculates the associated costs of an illness; this includes direct medical costs, lost wages and lost productivity time, as well as any lost earning of caretakers
Cost-Benefit Analyses	Looks at the costs and benefits of an intervention in monetary terms; can be expressed as net present value, ratio of benefits to cost, or economic rate of return
Cost-Effectiveness/ Cost-Utility Analyses	Provides information on the cost of an intervention and its "effectiveness" as defined by some non-monetary metric; These can include measures of Quality Adjusted Life-Years (QUALYS) or Disability Adjusted Life-Years (DALYS)

There have been numerous economic evaluations of onchocerciasis control programs over the years. Although they have differing results due to the time periods and regions evaluated, discount rates applied and the inclusion of different costs and benefits, they all conclude that onchocerciasis control programs have a high return on investment [1]. Two of the most comprehensive (and most cited) studies are cost-benefit analyses conducted by Kim & Benton of the World Bank. They calculated an economic rate of return (ERR) of 20% per year for the duration of the OCP, with 25% attributed to increased labor force and 75% to the increased land availability [22]. A 10% ERR is considered to be the standard of a successful development program by the World Bank [22,51]. The evaluation found that controlling onchocerciasis allowed communities to reclaim fertile lands that were once abandoned because of the high burden of disease. In all, 25 million hectares of land, enough to feed 18 million people, were made available for agriculture use again [1]. In Burkina Faso, 15 % of the country's land had been deserted and has since been reclaimed [17]. It is estimated that 3.7 billion dollars will be generated from increased land and agricultural productivity in these areas [1,17].

The ERR for APOC was estimated to be 17% a year by the World Bank. However, it should be noted that this cost benefit analysis was done using only the projected benefits from reductions in blindness and increases in land availability. It did not take into account the benefits from reductions in other manifestations of the disease, such as OSD, which has since been determined to represent a greater proportion of the DALYs. Also, it did not take into account direct medical costs associated with treatment for infected individuals [52]. Even without these additional benefits calculated, it was

estimated that every US dollar invested in the program, between 1996 and 2017, would add 27 productive workdays [22].

In a review conducted by Walter, Rehwinkel and Burnham of Johns Hopkins University, the ERR was found to be 20% for OCP and 24% for APOC [51]. They cited a recalculation of evaluation of the APOC done by Haddix in 1997 that included increased land use. Using a 10% discount rate to account for future gains in health and productivity, it was calculated that the OCP's net present value is $485 million and the APOC is $88 million, over a 39 and 21-year time period respectively [51]. Other evaluations indicate a net present value of $919 million over 39 years for the OCP and $121 million over 21 years for the APOC [13]. Net present value measures the difference between accrued and expected costs and benefits.

Recent studies estimate a DALY burden of onchocerciasis of 1.5 million a year [13]. However, it has been suggested that blindness should be given a greater disability weight since it affects the lives and productivity of caregivers as well [52]. Blindness is a major liability, both for the infected individual and their family. Since men of working age, who may be the breadwinner of the family, are most often affected, blindness can make an entire family vulnerable to poverty and hunger [27,53]. Cost effectiveness analyses found the cost per DALY prevented is between $14-$30; however, for APOC this is in large part due to the drugs being donated. None of the studies reviewed included the costs incurred by Merck, whose donation of Mectizan for just one year would outweigh the expected economic return. However, these cost benefit analyses only look at blindness as a health-related outcome and do not take into account the numerous other

benefits of ivermectin, including reduced musculoskeletal pain, getting rid of other parasites and allowing for nutritional gains [51].

The World Bank and the Institute of Pathobiology of the University of Addis Ababa conducted a study on the economic impact of OSD at the second largest coffee plantation in Ethiopia. Employees with severe OSD were found to earn 15% less in daily wages than their counterparts without the disease [52]. Those with OSD earned, on average, 29.7 Birr less than those without the disease, which represented 5.2% of the per-capita GDP in Ethiopia at the time. It was also found that those with OSD missed, on average, an additional 1.9 days of work compared to those without it [51] and spend more time seeking healthcare [1,52].

People affected by onchocerciasis also incur greater direct medical costs for treating the symptoms of their illness. Since NTDs thrive in areas of impoverishment, this added cost often represents a great percentage of their earnings and can push people into a "medical poverty trap," further exacerbating inequalities. This is a cycle in which people delay seeking assistance because of cost or stigma, which in turn drives up the cost of care since symptoms progress making treatment more difficult or impossible [13]. In 1997, the World Bank, UNDP, and WHO's Special Program for Research and Training in Tropical Diseases (TDR) conducted a multi-country study to look at the economic impact of OSD in Nigeria, Ethiopia and Sudan and found similar results. Those with severe OSD were found to spend, on average, an additional $20 per year on health expenditures, an amount which can represent as much as 15% of their annual income. Furthermore, those with OSD were found to spend more time in activities classified under 'sickness' and 'fatigue/weakness,' and less time in 'productive' and 'household'

activities. Specifically, they spent 6.75 extra hours seeking health care over 6 months compared to their non-OSD counterparts [27,51,52].

A review of the socio-economic impact of onchocerciasis conducted by Ubachukwu mentioned several other factors affecting productivity. For instance, pain from nodules (particularly around the hip) was associated with decreased farming activities. Also, severe scratching, which resulted in a loss of sleep, was shown to lessen productivity and affect absenteeism from work [27].

In a multi-country study in Cameroon, DRC, Nigeria and Uganda, 75.6% of the respondents listed work productivity and improved food security as social benefits of taking ivermectin. They reported that people in the community were able to spend more time tilling the land and were able to farm areas that used to be uninhabited. They believed that treatment with ivermectin enabled increased agricultural production for both the household consumption and marketplace sale. This study also illustrated how stigma and discrimination towards affected individuals had an economic impact, as they were not free to take on leadership roles or migrate for jobs:

> "The truth is that the difference is clear because about 5-6 years ago, it was becoming very embarrassing for us here because even in the market square, you would find people using sticks to scratch their legs or hands. There are some young people who could not go to the city to look for jobs because of their condition but if you look around now, only those that are still in secondary school can be found here in the village. The others have gone to the cities to look for work because they no longer have irritated skin to be ashamed of (male youth, Nigeria)" [54].

These studies illustrate how onchocerciasis can lead to decreased worker productivity and, in turn, decreased wages and agricultural output. Seeking treatment for the symptoms also has a direct medical cost. On the individual level, this can affect a

person's ability to save, invest, and hold or purchase capital. On the aggregate level, this can affect a region's economic development [13].

MDG 2: Achieve universal primary education

In reviewing the literature around education and onchocerciasis, there were consistent reports that onchocerciasis negatively affects school-aged children's school attendance and ability to concentrate in class.

A study conducted in the Taraba River Valley of Nigeria found that children under the age of 10 were already affected by onchocerciasis. Children, as young as five years old, already had skin lesions and some students had serious and irreversible eye lesions that were affecting their vision. Girls with lesions were reported to withdraw from social activities and school because of the stigma associated with the disease [29]. Another study, in Benue State of Nigeria, found that 30% of children aged 5 years, who were living in hyper endemic regions in the early 1990s, had some level of visual impairment due to onchocercal eye disease [27]. It was observed that constant itching distracted students, making learning more difficult, and that academic performance was negatively correlated with various manifestations of the disease [27].

A multi-country study in Ethiopia, Nigeria and Sudan found that the risk of dropping out of school was twice as high for children whose head of house had OSD compared to those uninfected. The study also found that girl children were more likely to be affected than boys [27,52]. In a multi-country study in Cameroon, DRC, Nigeria and Uganda, 28.5% of those surveyed said that, following treatment with ivermectin, school attendance was improved, as children did not have to leave school to take care of affected relatives. Interviews and focus groups with school managers and parents revealed that

children were able to focus more as their skin cleared and itching was alleviated. An interesting observation was that students who were thought to be epileptic saw improvements after taking ivermectin. Whether the finding was reliable, ivermectin did improve their social life as the students with epileptic seizures had previously been avoided and isolated [54].

An added benefit of MDA of ivermectin is that the drug is also effective against scabies and certain intestinal parasites. Studies have found that treating children with anti-helminthic medications increases appetite, weight and height, and leads to increases in school attendance [1]. Though difficult to determine the attributable affect of ivermectin in areas that are also treated for Soil-Transmitted Helminthes (STH), it is clear that people feel relief after treatment.

MDG 3: Promote gender equality and empower women

Most epidemiological studies show that men have higher microfilarial loads and consequently a greater burden of disease. This disparity is primarily considered to be due to men traditionally having more exposure to the black fly through their agricultural activities. However, due to demographic and historic changes, women in Africa now make a significant contribution to agriculture production and are consequently more susceptible to the bites of the black fly than in previous times [27]. Furthermore, while the prevalence of blindness is higher among men, a disproportionate burden of the disease falls on women and girls in relation to caretaking and stigma [18,29,33].

In many of the societies impacted by onchocerciasis, marriage is considered an important cultural rite of passage and can be central to female identity. OSD can be particularly damaging to females as suitability for marriage is often tied to a woman's

appearance and perceived reproductive abilities. A study by Ukpai and Ezeji found that women with the highest levels of onchocercal infection were single despite being of marriageable age [27]. *S*tudies in Nigeria have also shown that girls with skin lesions were avoided and married later in life [55].

Many mothers interviewed agree that onchodermatitis affects the marriage chances of young women because men want to marry 'pretty' women. They believed the disease affects women's future happiness, as it limits their prospects. If initially overlooked, women would be limited in their choice of husband to those who are widowed, divorced, disabled, or otherwise deemed less desirable. Also, in parts of West Africa, there is a cultural belief that the afflictions of a mother will also affect her children. Although onchocerciasis is not transmitted from mother-to-child, the belief that this occurs can be just as stigmatizing [27,56].

Another study found that girls were more likely to withdraw from social activities, including school, to avoid the shame associated with lesions. Women also appear to be affected by certain unique pathologies. For instance, some women develop a "hanging pouch of lymphadenomatous skin." People with such visible symptoms were determined to have low self-esteem, experienced embarrassment, and expressed less willingness to engage in community activities [29]. Stigma can also affect health-seeking behaviors as fear of being socially ostracized can keep people from going for treatment, which in turn allows the disease to progress [40].

Women are also disproportionately affected by onchocerciasis as they are traditionally the caretakers of the family [18]. A World Bank study found that girls were more often taken out of school to take care of a disabled relative than boys [52]. Since

people who are blind or have advanced visual impairment are left almost fully dependent on others for day-to-day activities, the caretaker's time and productivity is also diminished.

MDG 4: Reduce child Mortality

While this literature review did not find a link between child mortality and onchocerciasis, it also revealed that there is little research on the effects of infection in children. Onchocerciasis usually progresses over time, as repeated exposure to bites of infected flies increases an individuals' microfilarial load. Even so, it appears the disease affects the health of children under-five both directly and indirectly.

Children born to mothers who are infected with Onchocerca Volvulus were found to be at higher risk of onchocerciasis, became infected earlier in life and had higher levels of microfilaria throughout the observation period [57,58]. Though this relationship could be confounded by environmental and/ or behavioral factors, it is suspected to be due, in part, to prenatal priming of the immune system. Transplacental migration of larvae, evidenced by microfilariae found in fetal tissue, may modify the developing fetus' immune response [58].

While microfilarial prevalence tends to increase with age, as it is related to the level and frequency of exposure, all people in endemic areas are at risk. A study that looked at the prevalence of microfilaria in children 0-4 years in South East Nigeria found that 15.7% of the sample population was infected, demonstrating that that infection is acquired early in life. Young children are more likely to develop nodules on the head, probably since they are closer to the ground than adults, and this may put them at greater risk of developing ocular impairment. Also, since they are not treated during MDA, they

can act as a reservoir for the parasite [2,25,59]. Even more significant is the growing body of evidence supporting a relationship between helminth infections and impaired immune response. This means that children with higher levels of infection could be more vulnerable to other diseases, such as malaria and diarrheal disease, which are major killers of under-fives [57,60,61].

Nutritional status may also be indirectly affected by onchocerciasis via two routes. First, onchocerciasis infection appears to have a harmful effect on breastfeeding duration as women experience aggravated pain and itching around the breast [22,27]. A study conducted in the rainforest areas of Nigeria found that 73% percent of women with onchocerciasis infection experienced itching during breastfeeding. Of the women who breastfed before and after the onset of itching, 25% weaned their children 9 months early. A regression model showed that severity of lesions could be a predictor for duration of breastfeeding [55]. Secondly, children with parents who suffer from onchocerciasis may be more likely to live in food insecure homes. As discussed under MDG 1, there are many studies that show the correlation between infection and decreased agricultural productivity and income.

MDG 5: Improve Maternal Health

Although onchocerciasis programs arguably improve maternal health, they do not have any real impact on the indicators used to measure progress in this area, which focus on maternal mortality and access to reproductive health services. The only case that could plausibly be made is that the outside work of some community directed distributers (CDDs) supports access to reproductive health. However, while many CDDs have taken

part in family planning activities, there is no data available on the quality or extent of those services.

Onchocerciasis does appear to have certain pathologies that are unique to women. Studies in Ecuador, Tanzania, Mali, and Nigeria found that many women believe onchocerciasis is responsible for infertility, spontaneous abortion and stillbirth; however, there is no evidence to support this theory [29,38,56]. Onchocerciasis symptoms do seem to be exacerbated during pregnancy as women sometimes develop more severe skin lesions and the "deterioration of papular/pustular eruptions." It is unclear if these pathologies result from hormonal changes or immune-suppression. Though there are a few studies that have looked at the effect of onchocerciasis in relation to pregnancy and other reproductive function, there is a lack of longitudinal studies that look at lifetime impact on women [29].

It is theorized that high microfilarial loads weaken the immune system, leaving the human host more vulnerable to other infections. An intense infection may also cause systemic effects such as epilepsy, growth retardation and general debilitation [23,36,57]. Although microfilariae have been found in most major organs during autopsy, there is no evidence that this causes impairment of organ function [29].

Poor nutritional status also may contribute to excess mortality. Some people with high microfiliaral loads present with wasting, including loss of adipose tissue and muscle mass [29]. In a study looking at "subjective complaints and measureable morbidity" in Malawi, there was a statistically significant correlation between weight and onchocerciasis infection. Both blind and sighted women who tested positive for onchocerciasis infection weighed less than their non-infected counterparts. Women with

normal vision that had positive skin snips weighed, on average, 1.6kg less than whose with negative skin snips, while women who were blind weighed, on average, 6.8 kilograms less than women with normal vision [1,29].

MDG 6: Combat HIV/AIDS, malaria and other diseases

The onchocerciasis programs most directly addresses goal number 6 by controlling and eliminating a debilitating infectious disease. There are a host of reports that highlight the successes of OCP, APOC and OEPA including eliminating selected breeding sites and treating millions of people with ivermectin so they no longer suffer from the worst manifestations of the disease and are able to reclaim fertile lands for agriculture use. However, the programs are also credited with the development of the Rapid Epidemiological Mapping of Onchocerciasis (REMO) tool, the technique of community-directed distribution, and developing one of the most successful public-private ventures ever undertaken, the Mectizan Donation Program (MDP). These ancillary developments have strengthened health systems and opened-doors for other health and development programs [17,62,63].

The CDTI system has provided opportunities for integration with other health programs. CDDs have been involved in many of health activities including the Expanded Program on Immunization (EPI), malaria bed-net distribution and at-home treatment, vitamin A distribution, and family planning counseling. In 2012 alone, more than 47 million treatments and commodities were delivered through the network of trained CDTI volunteers, supporting 13 other health interventions [21]. This is not only seen as a benefit by health officials, but also by community members. In a multi-country study in Cameroon, DRC, Nigeria and Uganda, one of the perceived benefits of onchocerciasis

control was the access to health education provided by CDDs [54]. Integrating ivermectin distribution with other health services is not only possible, but it has been shown to increase uptake/coverage and make programs more sustainable [64-66]. A pilot study in Nigeria found that integrating delivery of Vitamin A with ivermectin distribution increased coverage rates substantially. When Vitamin A was delivered through traditional health service's facilities, coverage rates ranged from zero to 30 percent, but when co-distributed with ivermectin, average rates were 80 percent [45]. The WHO conducted a three-year multi-country study to look at how the CDTI strategy might be used with other health interventions alongside ivermectin distribution and also found it to be much more effective than the regular delivery methods for malaria treatment, bed nets for malaria prevention, and vitamin A distribution. The additions to CDTI not only enhanced coverage for the add-ons, but the onchocerciasis programs also saw coverage increases of 10%. The only intervention that did not show significant improvement was the Directly Observed Treatment of Tuberculosis short course (DOTS), but integration didn't impede either program [66]. The kinship model, piloted in Uganda, which has CDDs distribute to their relatives, has shown even better results in terms of coverage [67]. Furthermore, when drug delivery for NTD control is integrated, studies have found significant cost-savings [68,69].

The CDTI strategy has strengthened the health system in countries where it exists by creating and strengthening distribution lines. In particular, it provides a viable entry point into remote and conflict-affected areas which are otherwise hard to reach [8]. For example, in the Central African Republic, the community distributors are some of the only health workers who reach all villages [17]. CDDs have also played a valuable role in

operational research and national surveillance [14]. For example, the APOC has enlisted CDDs to gather data including the latitude and longitude of each village, and health center and the demographic characteristics of households in 32,000 communities. This information will be valuable to many other programs and studies [48]. In 2012, over 650,000 CDDs were trained or re/trained in 22 countries, as were over 80,000 health workers in 20 countries [21].

In addition to the benefits of CDTI system, onchocerciasis control and elimination may contribute to the overall health of affected populations. In sub-Saharan Africa, the same population that is affected by HIV, TB and malaria are often polyparasited with NTDs [1]. Research is now showing that NTDs make people more susceptible to the "big three" and that co-infection may worsen outcomes for patients [1,8,68]. In particular, helminth infections are thought to weaken immune response and may impair the ability to seroconvert after vaccination [23,61].

Treatment with ivermectin also confers secondary benefits. [70,71]. While albendazole is now the recommended drug for STHs, ivermectin has a "significant effect" on Ascaris and Trichuris and is the "drug of choice" for human strongyloidiasis [8]. It is also almost 100% effective against round worms and whipworms [17]. MDA has shown a reduction in prevalence of ectoparasitic skin infections such as pediculosis, tungiasis, scabies, and cutaneous larva migrans. The reduction in scabies in turn reduces secondary skin infections, as well as post-streptococcal glomerulonephritis, which can cause renal disease [8]. Ivermectin has proved to be a popular drug because people feel immediate relief from itching associated with onchocerciasis, as well as relief from other parasites including intestinal worms, scabies, and head lice [17]. In a multi-country study

in Cameroon, DRC, Nigeria and Uganda, the community believed the drug improved their overall social, psychological and economic well-being [54].

MDG 7: Ensure environmental sustainability

In reviewing the indicators for MDG 7, it was determined that the onchocerciasis programs do not make any contribution towards achieving this goal. However, it can be noted that the program does make use of environmentally safe insecticides in the few areas that use vector control as a strategy. Thus, these programs do not inhibit the achievement of this goal in any noticeable way.

MDG 8: Develop a global partnership for development

The APOC is an exemplary illustration of the global partnerships envisioned in MDG 8. This partnership has included the WHO, UN, World Bank, FAO, the pharmaceutical company Merck, 31 African countries, 21 bilateral and multilateral donors, over 20 international and local NGOs, and over 190,000 endemic communities [17,21].

In 1975, Dr. William Campbell, a veterinary researcher at Merck & Co, discovered the first endectocide and anthelmintic drug, ivermectin. While it was originally intended to treat gastrointestinal worms in cattle and horses, it was found to be efficacious and safe for use in humans as well [2,17]. Merck was willing to donate the drug if a partner could manage its distribution. Dr. William Foege, then Executive Director of The Carter Center, took on the challenge of leading the MDP once Merck pledged its long-term support [17]. In 1987, Merck began donating ivermectin (under brand name, Mectizan®) for “as long as needed” to help fight river blindness [2]. Merck bears the cost of production, transport to the port of entry, and any clearing costs, while

the MDP manages administration and distribution of the drugs to the entities responsible for implementation of the programs [51]. The MDP is overseen by the Mectizan Expert Committee, which is made up of tropical disease experts from the WHO, CDC and Merck scientists [51].

Specifically, target 8E states, “in cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries” [7]. Merck has calculated the value of each tablet to be $1.50, which would put their donation, over the past twenty years, over two billion dollars [51,62]. In 1998, Merck extended its donation to include treatment for Lymphatic Filariasis (LF) which requires treatment with both ivermectin and albendazole (donated by GlaxoSmithKline) [17].

The Mectizan Donation Program was the first of its kind and paved the way for similar programs. It is the longest running drug donation program and continues to be one of the largest public-private partnerships ever created [17]. Merck’s long-term commitment was vital and is one of the key reasons for the success of the onchocerciasis programs. It allowed governments and NGOs the time to invest in operational research and learn from years of experience, without the threat of the programs’ end or need to source other funds [17].

Research Questions

Research Objective

The objective of this research is to illustrate how the control and elimination of onchocerciasis contributes to achievement of the current MDGs. The term "contribute" was chosen for the analysis as it allows the full scope of benefits to be evaluated without suggesting a causal link. Onchocerciasis programs and MDGs employ different indicators to measure progress, making it impossible to quantify a direct impact on MDGs. Also, since MDGs are national indicators and onchocerciasis programs are only present in endemic foci, which often face a host of obstacles to development, it is not feasible to parse out or prove that benefits achieved at the local level are seen at a national level. Nevertheless, this project will look for correlations between onchocerciasis control and MDG indicators. Specifically, program data and evidence from previous studies will be drawn upon to demonstrate how onchocerciasis programs contribute toward select MDG targets. While the association is not quantifiable, the project aims to demonstrate the impact of these programs across multiple markers of development.

Research Questions

- What indicators can be used to demonstrate the impact of onchocerciasis control and elimination programs?
- Are these programs making a contribution towards the achievement of specific MDGs?

Methodology

A review of literature and data on the subjects of onchocerciasis and the MDGs was conducted in four stages. This included the examination of peer reviewed articles,

grey literature, and program reviews, as well as utilizing publicly available databases to search for country statistics and indicators of development.

First, a basic search on onchocerciasis/ river blindness was conducted to explore pertinent topics and learn about the pathology and epidemiology of the disease.

Second, a review of the MDGs and indicators was conducted to understand their history and purpose, as well as their utility in measuring development progress. Analyses from the UN Statistics Division, Center for Global Development, Overseas Development Institute and African Development Bank were used to assess MDG progress among onchocerciasis endemic countries. Recognizing the limitations of national comparisons of MDG progress alone, these organizations developed various alternative measures of progress, in relation to MDG indicators, that were used in this analysis:

Table 4: MDG Progress Terms

MDG PROGRESS TERMS	
Absolute Progress; Overseas Development Institute, 2010	Measures overall gains (i.e. "which countries have reduced the largest share of the population living in extreme poverty, for instance, or increased primary school enrollment rates by the largest number of percentage points")
Relative Progress; Overseas Development Institute, 2010	Measures progress against MDG targets (i.e. "which countries have come closest to halving child mortality, or to closing the gap in achieving universal primary education")
Accelerating Progress; African Development Bank, 2012	Measures effort towards goal by quantifying the rate of change, from baseline to the current year, for a given indicator.
Progress Index, Center for Global Development, 2010	Ranks countries by overall progress towards MDGs; looks at eight indicators that cover seven goals; countries are given a score between 0 and 1 for each goal so a score of 8 would imply they are on track for reaching all goals and a zero would mean they are not on track to meet any (see appendix for scores).

Third, a search of onchocerciasis in relation to each of the MDGs was conducted to see what literature exists on the subject. Pubmed, Wed of Science and Cab Direct were used to search the terms "onchocerciasis AND river blindness" in combination with the following key words: "MDGs," "poverty," "economics," "malnutrition," "food insecurity," "education," "helminth infections," "children," "school attendance," "women," "gender," "gender equity," "stigma," "maternal health," "reproductive health," "mortality," "loa loa," "environment," "HIV," "partnerships," "ivermectin," "Mecitzan Donation Program," and "community directed." Abstracts and full articles were reviewed if they addressed any of the MDG goals or targets. The reference sections of key sources were used to identify primary studies and other relevant articles.

Fourth, websites and reports from organizations that manage and/or implement onchocerciasis programs were reviewed in order to understand operating procedures and assess the collective reach of current onchocerciasis partners. These included but were not limited to: WHO's website (including APOC's annual program reports and the Joint Action Forum newsletters), The Carter Center's website, internal databases and program reviews, and the MDP's website. Data from these sources were compiled in a spreadsheet to demonstrate the progression and magnitude of these programs; this includes information on levels of endemicity, number of people at risk, number of people treated, annual therapeutic and geographic coverage levels, number of community directed distributors and health workers trained, non-program specific activities undertaken by community directed distributors, and the number of drugs donated by Merck.

In order to answer the research questions, data from the reviews that illustrate the impact of onchocerciasis programs were populated into a table divided by MDG targets and indicators (See table 5 for results and the appendix for all MDG indicators). An MDG was selected for inclusion if any of its indicators appeared to be hindered by the presence of onchocerciasis or impacted by its control. Likewise, if no relationship was seen for all indicators, the MDG was excluded. Using these criteria, Goal 5 (Improve Maternal Health) and Goal 7 (Ensure Environmental Sustainability) were excluded. Lastly, to see if any correlation exists between the success of onchocerciasis programs and MDG progress, country progress was compared to levels of 2012 therapeutic coverage.

Selection of MDG Indicators

After reviewing the impact of onchocerciasis programs, the following MDG indicators were deemed relevant to onchocerciasis programs: Proportion of population below $1 (PPP) per day (MDG 1.1); Growth rate of GDP per person employed (MDG 1.4); Prevalence of underweight children under-five years of age (MDG 1.8); Proportion of population below minimum level of dietary energy consumption (MDG 1.9); Net enrollment ratio in primary education (MDG 2.1); Ratio of girls to boys in primary, secondary and tertiary education (MDG 3.1); Under-five mortality rate (MDG 4.1); Infant mortality rate (MDG 4.2); Incidence of death rates associated with malaria (MDG 6.6); Proportion of children under 5 sleeping under insecticide-treated bed nets (MDG 6.7); Proportion of children under 5 with fever who are treated with appropriate anti-malarial drugs (MDG 6.8); Incidence, prevalence and death rates associated with

tuberculosis (MDG 6.9); Proportion of population with access to affordable essential drugs on a sustainable basis (MDG 8.13).

Geographic Focus

This paper reviews the efforts to control and eliminate onchocerciasis globally. This includes the 31 countries included in the Onchocerciasis Control Program (OCP) and its successor, the African Program for Onchocerciasis Control (APOC): Benin, Burkina Faso, Cote d'Ivoire, Ghana, Guinea Bissau, Guinea, Mali, Niger, Senegal, Sierra Leone, Togo, Angola, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Ethiopia, Equatorial Guinea, Gabon, Kenya, Liberia, Malawi, Mozambique, Nigeria, Rwanda, Sudan, South Sudan, Tanzania, Uganda; and the six Central and South American countries of the Onchocerciasis Elimination Program of the Americas (OEPA): Brazil, Ecuador, Guatemala, Mexico, Venezuela and Colombia. Although Yemen has an onchocerciasis program, it has been excluded from this review due to lack of publicly available data.

Limitations

There are a number of data limitations that make measuring progress towards MDGs challenging. To start, there are very limited baseline data, making it difficult to measure change over time. For instance, nearly half of countries in sub-Saharan Africa do not have data on hunger and poverty for 1990 [72]. Moreover, the 60 indicators chosen to measure progress were not formally agreed upon, but were outlined in the "Roadmap towards the Implementation of the United Nations Millennium Declaration" in 2001 [73] and, as a result, there is not consistency among countries in what indicators are reported [74]. While data management systems have improved significantly in many parts of the

world, there are still areas, particularly those affected by conflicts, which have spotty and inconsistent data, and issues of data retraction have led to volatility in annual reports [72,74].

There is also reason to question if using the MDGs as a benchmark produces the most accurate picture of the state of affairs. For instance, there are concerns that the indicators chosen do not provide the best measure for the intended outcomes, and that others, such as maternal mortality, are too difficult to measure. Even disregarding this structural issue, criticisms around the utility of the data that are reported are valid. While the UN and World Bank keep extensive information on each indicator in online databases, the level of detail is not of much use to the average stakeholder. In an attempt to provide user-friendly data, UN country reports over-simplify; each goal is marked as "achieved," "on track," "off track," or "possible to achieve with changes." Since this data is aggregated at the national level, progress in one subset of the population can mask inequalities [72]. This is also true on the regional scale; while "snapshots" of select indicators give a good indication of large-scale change, they can misrepresent the status of smaller countries. For instance, due to the size of Nigeria and the Democratic Republic of Congo, reports of sub-Saharan Africa are heavily skewed in their direction, hiding the progress of some smaller neighbors. Likewise, accelerated progress in China makes Eastern Asia appear as though it is on track for reaching all goals, when there are considerable disparities between countries. For all that, MDG data are still the best available to compare and monitor progress globally. Expert agencies, recognizing the information gap, have analyzed the data on specific regions and topics to provide more holistic and accurate measures of development [74].

Onchocerciasis programs have extensive data, but what is publicly available through the WHO is limited to the numbers of people living in meso/hyper endemic areas as of the last REMO activity (typically 2006) and annual treatment data. Though the date each country's first CDTI program was launched is indicated on APOC's website, the number of years each country has met the necessary therapeutic coverage level is not. Furthermore, since control and elimination are the priority of these programs, there is little recent research on the numbers of people affected by the various associated morbidities.

Even without these limitations, a causal link between onchocerciasis control and MDG progress is not plausible. Onchocerciasis occurs in specific geographic foci, which may only affect a small percentage of the population, while the MDGs are national. Also, onchocerciasis occurs primarily in settings of poverty where people face a host of obstacles to development. There are also issues of confounding that are unaccounted. For one, it is unknown what other health and development programs were implemented in these areas. Moreover, the countries with endemic onchocerciasis not only have different vectors and different degrees of disease burden, but they also have vastly different political and economic environments.

CHAPTER III: MANUSCRIPT

TITLE: Retrospective Review of Onchocerciasis Control and Elimination Program Contributions to the Achievement of the Millennium Development Goals

Dunn C (1,2) and Callahan K (1), Katabarwa M (1), Richards F (1), Hopkins D (1), Ngondi J (1,3), Buyon L (1), McFarland D (2)

1. The Carter Center, Atlanta, GA USA
2. Hubert Department of Global Health, Emory University, USA
3. Department of Public Health and Primary Care, University of Cambridge, UK.

Caitlin Dunn cdunn3@emory.edu
Kelly Callahan ecallah@emory.edu
Moses Katabarwa mkataba@emory.edu
Frank Richards frank.richards@emory.edu
Donald Hopkins sdsulli@emory.edu
Jeremiah Ngondi jn250@cam.ac.uk
Lucas Buyon lucas.buyon@emory.edu
Deborah McFarland dmcfarl@emory.edu

Key Papers in the Field:

Norris J, Adelman C, Spantchak Y, Marano K (2012) Social and Economic Impact Review on Neglected Tropical Diseases Washington, DC: The Hudson Institute. 36 p.

Benton B (1998) Economic Impact of Onchocerciasis Control Through the African Programme for Onchocerciasis Control: an Overview. Annals of Tropical Medicine & Parasitology 92: 8.

Ubachukwu PO (2006) Socio-Economic Impact of Onchocerciasis with Particular reference to Females and Children: A review Animal Research International 3: 11.

Hotez P, Ottesen E, Fenwick A, Molyneux D (2006) The Neglected Tropical Diseases: The Ancient Afflictions of Stigma and Poverty and the Prospects for their Control and Elimination. In: Pollard AJ, Finn A, editors. Hot Topics in Infection and Immunity in Children. New York: Springer. pp. 11.

National Research Council (1996) In her lifetime: female morbidity and mortality in sub-Saharan Africa: The National Academies Press.

World Health Organization (2008) Community Directed Interventions for Major Health Problems in Africa Switzerland.

Abstract:
In 2000, 189 member states of the United Nations (UN) developed a plan for peace and development, which resulted in eight actionable goals known as the Millennium Development Goals (MDGs). Since their inception, the MDGs have been considered the international standard for measuring development progress and have provided a blueprint for global health policy and programming. Yet, emphasis upon the achievement of priority benchmarks around the big three - namely HIV, TB and malaria - has influenced global health entities to disproportionately allocate resources. Meanwhile, several tropical diseases that almost exclusively impact the poorest of the poor continue to be neglected, despite the existence of cost-effective and feasible methods of control and elimination. One such Neglected Tropical Disease (NTD), onchocerciasis, more commonly known as river blindness, is a debilitating and stigmatizing disease primarily affecting individuals living in remote and impoverished areas. Onchocerciasis control is considered to be one of the most successful and cost-effective public health campaigns ever launched. In addition to improving the health and well-being of millions of individuals, these programs also lead to improvements in education, agricultural production, and economic development in affected communities. This paper reviews the contributions that such concentrated efforts to control and eliminate onchocerciasis make to achieving select MDGs. The authors hope to draw the attention of public policymakers and global health funders to the role onchocerciasis and other NTDs play in hindering development and advocate for their inclusion in the post 2015 agenda.

Introduction

As the 2015 deadline to achieve the Millennium Development Goals (MDGs) nears, it is timely to assess progress and consider priorities being set for the post-2015 agenda. Although data limitations have led to some concerns over their utility in gauging the equity and sustainability of achievements [3-6], the MDGs are considered to be the international standard for measuring progress. Moreover, since their inception, the MDGs have guided global health policy and programming, as they illustrate the link between population health and development more broadly [6,8]. This association is nowhere more evident than in the impact of Neglected Tropical Diseases (NTDs) on the world's poorest populations. As both proxies for and promoters of poverty, NTDs act as an impediment to human development; hence, a concerted effort to control and eliminate these diseases would make an indelible mark on the MDGs [20].

Of the major NTDs, onchocerciasis is one of the most common and costly. It is endemic to 31 African countries as well as 6 countries in the Americas and several areas in Yemen, putting over 100 million people at high risk of onchocerciasis infection worldwide [21]. Of the estimated 37 million people currently infected, 99% live in sub-Saharan Africa [22,23]. Onchocerciasis is transmitted by biting black flies, of the genus

Simulium, found near the fast flowing waters in which they breed – hence its common name, river blindness. When taking a blood meal, the black fly deposits infective larvae of a nematode worm, Onchocerca Volvulus, into its human host [24]. Upon maturation, females release thousands of embryos, called microfilariae (mf), per day, for the duration of their 9-11 year reproductive lifespan [22,24,25]. When the mf die, they invoke an inflammatory immune response; this repeated reaction destroys tissue and causes damage to the eyes, skin and possibly the brain [26].

Onchocerciasis is the second leading infectious cause of preventable blindness [1]. It causes an array of serious morbidities, including intense itching, Onchocercal Skin Disease (OSD), musculoskeletal pain and general malaise, weight loss, and 'hanging groin' or elephantiasis of the genitals. It is further suspected to be a cause of epilepsy [26,27,32,34]. Beyond health, onchocerciasis leads to grave social and economic consequences that exacerbate poverty and hinder overall development [1,27,52].

Efforts to control onchocerciasis through weekly aerial spraying of larvicides began in West Africa in the early 1970s under the management of the Onchocerciasis Control Program (OCP). This initiative was extremely successful, eliminating onchocerciasis as a disease of public health importance from 10 of the 11 OCP countries [2,22]. With the discovery of a safe and effective microfilaricide, ivermectin (brand name Mectizan), and its subsequent donation in 1987 by the pharmaceutical company Merck, onchocerciasis control was expanded to endemic countries in Central and East Africa under the management of the African Programme for Onchocerciasis Control (APOC) as well as the 13 endemic foci in Central and South America through the Onchocerciasis Elimination Program of the Americas (OEPA) [2,48]. The disease is now controlled primarily through Mass Drug Administration (MDA) of ivermectin; one dose kills 95% of the larvae, relieving most of the symptoms and temporarily reducing reproduction, thus slowing transmission [22]. Elimination programs are beginning to implement semi-annual MDA as it has been shown to shorten the life span of the adult worm significantly [42].

Methods

To determine the impact onchocerciasis control and elimination programs have on the MDGs, the authors conducted a literature search using Pubmed, Web of Science and Cab Direct. The terms "onchocerciasis AND river blindness" were searched in combination with the following key words: "MDGs," "poverty," "economics," "malnutrition," "food insecurity," "education," "helminth infections," "children," "school attendance," "women," "gender," "gender equity," "stigma," "maternal health," "reproductive health," "mortality," "loa loa," "environment," "HIV," "partnerships," "ivermectin," "Mecitzan

Donation Program," and "community directed." Abstracts and full articles were reviewed if they addressed any of the MDG goals or targets. The reference sections of key sources were used to identify primary studies and other relevant articles. Additionally, publicly available data from APOC and the Mectizan Donation Program and reports from organizations that manage onchocerciasis programs were reviewed to assess the collective reach of current onchocerciasis partners.

These findings were populated into a table divided by MDG targets and indicators (See Table 5). An MDG was selected for inclusion if any of its indicators appeared to be hindered by the presence of onchocerciasis or impacted by its control. Using this criterion, Goal 5 (Improve Maternal Health) and Goal 7 (Ensure Environmental Sustainability) were excluded, as there was no evidence of an association with any indicators. Analyses from the UN Statistics Division, Center for Global Development, Overseas Development Institute and African Development Bank were used to assess MDG progress among onchocerciasis endemic countries. However, since the MDGs are national indicators and onchocerciasis programs are only present in endemic foci, which often face a host of obstacles to development, it is not feasible to parse out or quantify the degree that benefits achieved at the local level accrue to a national level. While not quantifiable, this article presents associations based on impact studies, economic evaluations and qualitative reviews.

Results

A literature and data review found that reducing the burden of onchocerciasis in highly endemic areas through control and elimination programs contributes to the achievement of select MDGs. This impact is explained in detail below and summarized in table five.

MDG 1: Eradicate extreme poverty and hunger

The initial epidemiological research into the extent of onchocerciasis in West Africa found the socio-economic consequences of the disease to be devastating. Over 60 percent of the savannah population was infected, half of the men over the age of 40 were blind, and the disease was already affecting children [22]. In an attempt to escape this scourge, entire villages moved away from the fertile river valleys that were home to the black fly. Living in over-crowded villages with poor soil and little access to water, agriculture yields were reduced, and subsequently, families were pushed further into poverty [22].

Research demonstrates that onchocerciasis exacerbates poverty in three main ways: by decreasing worker productivity and earnings, reducing agricultural yields, and increasing medical expenses [51,52]. A study on the economic impact of OSD at the second largest coffee plantation in Ethiopia found that employees with severe OSD

earned 15% less in daily wages and missed, on average, an additional 1.9 days of work per month [51,52]. The difference in income represented 5.2% of the per-capita GDP at the time [51]. Exhaustion from sleep deprivation and musculoskeletal pain were found to impact productivity and absenteeism [1,27].

Individuals with onchocerciasis also spend more time and money seeking healthcare [1,52]. A multi-country study in Nigeria, Ethiopia and Sudan found that those with severe OSD devote, on average, an additional $20 per year to health expenditures - up to 15% of their annual income. They were also found to spend more time in activities classified under 'sickness' and 'fatigue/weakness,' and less time in 'productive' and 'household' activities. On average, they spent 6.75 extra hours seeking health care over 6 months compared to their non-affected counterparts [27,51,52]. These added costs can push people into a "medical poverty trap," further widening inequalities [13].

Measuring the burden imposed by onchocerciasis using Disability Adjusted Life Years (DALYs) reveals its cost in healthy life to be 1.5 million years [13]. It should be noted that this number, large as it is, does not take into account the social ramifications of blindness. Individuals with advanced visual impairment become almost fully dependent on others, diminishing caretaker productivity as well [52]. Moreover, since men of working age are most often affected, blindness can make entire families vulnerable to poverty and hunger [27,53].

There have been numerous economic evaluations of onchocerciasis control programs, all of which conclude that they have a high return on investment [1,51]. One of the most comprehensive analyses, conducted by the World Bank, calculated an economic rate of return (ERR) of 20% per year for the duration of the OCP, with 25% attributed to increased labor force and 75% to the increased land availability [22]. A 10% ERR is considered to be the standard of a successful development program [22,51]. The evaluation found that controlling onchocerciasis in West Africa allowed communities to reclaim 25 million hectares, enough land to feed 18 million people [1].

The World Bank estimated the ERR for APOC to be 17% a year. However, this was calculated using only the projected benefits from reductions in blindness and increases in land availability. It did not take into account benefits from reductions in other morbidities, such as OSD, which represents a larger portion of the DALY burden in the region [22,52]. Even so, it was estimated that every US dollar invested in the program, between 1996 and 2017, would add 27 productive workdays [22]. The findings of these economic evaluations are supported by the experiences of affected communities. For instance, 75.6% of the respondents in Cameroon, DRC, Nigeria and Uganda listed work productivity and improved food security as benefits of taking ivermectin [54].

These studies compellingly illustrate not only that onchocerciasis can affect a region's economic development by debilitating the workforce and reducing land utility, but also that control programs can reverse the situation.

MDG 2: Achieve universal primary education

Onchocerciasis begins to take its toll in early childhood. In the early 1990s, in the Benue State of Nigeria, 30% of children aged 5 years and living in hyperendemic regions had some level of visual impairment due to onchocercal eye disease [27]. Another study, conducted in the Taraba River Valley of Nigeria, found that children as young as five had skin lesions and some students had irreversible eye lesions affecting their vision [29]. Academic performance was found to be negatively correlated with infection as constant itching, insomnia, and fatigue affected student's ability to focus [27].

A World Bank study found the risk of dropping out of school was twice as high for children whose head of house had OSD and girls were more likely to be taken out of school to care for a disabled relative than boys [52]. Following treatment with ivermectin, nearly a third (29%) of those surveyed in Cameroon, DRC, Nigeria and Uganda mentioned that school attendance improved, as fewer children left school to care for sick relatives. Interviews and focus groups with school managers and parents revealed that children were able to focus more as their skin cleared and itching was alleviated [54].

An added benefit of MDA is that ivermectin is also effective against scabies and certain intestinal parasites [8,17,70]. Studies have found that treating children with anti-helminthic medications increases appetite, weight and height, and leads to increases in school attendance [1]. Though difficult to determine the attributable effect of ivermectin in areas that are also treated for Soil-Transmitted Helminthes (STH), it is clear that students feel relief after treatment.

MDG 3: Promote gender equality and empower women

Due to demographic and historic changes, women in Africa now make a significant contribution to agriculture production and are consequently more susceptible to the bites of the black fly than previously [27]. More importantly, a disproportionate burden of the disease falls on women and girls in relation to caretaking and stigma [18,29,75].

In many societies marriage is considered an important cultural rite of passage and can be central to female identity. By causing skin deformities, OSD damages marriage prospects, and is, as a result, perceived to affect a woman's future happiness [75,76]. In fact, in parts of Nigeria, onchodermiatitis is known as 'osepuru nwanyi aka na di' or the disease that 'prevents a girl from getting married' [77]. These concerns are validated by studies that found women with the highest levels of onchocercal infection were more likely to be single despite being of marriageable age [27], and that girls with skin lesions were avoided and married later in life [55].

Cultural beliefs about disease etiology also contribute to the ostracism of infected women. In parts of West Africa, it is believed that the afflictions of a mother will be passed to her children [27,77]. Studies in both South America and Africa found many

people believe onchocerciasis causes reproductive complications including spontaneous abortion, stillbirth and infertility [29,38]. While not substantiated with evidence, these beliefs still have bearing as a woman's perceived reproductive abilities are considered important in assessing suitability for marriage [39].

In addition to facing these negative cultural responses, women with onchocerciasis also appear to be affected by unique pathologies. For example, some women develop a "hanging pouch of lymphadenomatous skin." Women with such visible symptoms have low self-esteem, experience embarrassment, and avoid community activities [29]. Though stigma affects both genders, girls are more likely to withdraw from social activities, including school, to avoid the shame associated with lesions [76]. Stigma also affects health-seeking behaviors as fear of being socially ostracized can keep people from going for treatment, which in turn allows the disease to progress [40,41].

MDG 4: Reduce child mortality

Children born to infected mothers were found to be at higher risk of developing onchocerciasis, became infected earlier in life and had higher levels of microfilaria [57,58]. Though this relationship could be confounded by environmental and/or behavioral factors, it is suspected to be due, in part, to prenatal priming of the immune system. Transplacental migration of larvae, evidenced by microfilariae found in fetal tissue, may modify the developing fetus' immune response [58]. A growing body of evidence supports a relationship between helminth infections and impaired immune response. This means that children with higher levels of infection could be more vulnerable to other diseases, such as malaria and diarrheal disease, which are major killers of under-fives [57,60,61]. An intense infection may also cause systemic effects such as epilepsy, growth retardation and general debilitation [23,57].

Onchocerciasis may also indirectly affect nutritional status in two ways. First, onchocerciasis infection appears to have a harmful effect on breastfeeding duration as women experience aggravated pain and itching around the breast [22,27]. A study conducted in the rainforest areas of Nigeria found that 73% percent of infected women experienced itching during breastfeeding. Of the women who breastfed before and after the onset of itching, 25% weaned their children 9 months early. A regression model showed that severity of lesions could be a predictor for duration of breastfeeding [55]. Second, children with parents who suffer from onchocerciasis may be more likely to live in food insecure homes; as discussed under MDG 1, many studies show a correlation between infection and decreased agricultural productivity and income.

MDG 6: Combat HIV/AIDS, malaria and other diseases

The onchocerciasis programs most directly address goal 6. A host of reports highlight the successes of OCP, APOC and OEPA including the elimination of select

breeding sites, and treatments that have alleviated the worst manifestations of the disease for millions. However, the success of these programs extends beyond disease specific endeavors. These programs have also contributed to the development of the Rapid Epidemiological Mapping of Onchocerciasis (REMO) tool, the technique of Community-Directed Distribution, and one of the most successful public-private partnerships, the Mectizan Donation Program (MDP). These ancillary developments have strengthened health systems and opened doors for other health and development programs [17,62,63].

The Community Directed Treatment with Ivermectin (CDTI) system has provided countless opportunities for integration with other health programs. Already, Community Directed Distributors (CDDs) have been involved in health activities such as the Expanded Program on Immunization (EPI), malaria bed-net distribution and at-home treatment, Vitamin A distribution and family planning counseling. In 2012 alone, more than 47 million treatments and commodities were delivered through the CDTI network, supporting 13 additional health interventions [78].

Integrating ivermectin distribution with other health interventions is not only possible, but it increases uptake and coverage, decreases costs and makes programs more sustainable [64-66,69]. A pilot study in Nigeria found that integrating delivery of Vitamin A with ivermectin distribution increased coverage rates substantially - from zero to 30 percent to an average of 80 percent [45]. The WHO conducted a three-year multi-country study that also found integrated delivery with ivermectin is more effective than the regular delivery methods for malaria treatment, Insecticide Treated mosquito Nets (ITNs) and Vitamin A distribution. The additions to CDTI not only enhanced coverage for the add-ons, but the onchocerciasis programs also saw increases of 10% [66]. The kinship model, piloted in Uganda, which has CDDs distribute to their relatives has shown even better results in terms of coverage [67]. Furthermore, when drug delivery for NTD control is integrated, studies have found significant cost-savings [68,69].

The CDTI strategy has strengthened health systems by creating and strengthening distribution lines. In particular, it provides a viable entry point into remote and conflict-affected areas [8]. For example, in the Central African Republic, community distributors are some of the only health workers who reach all villages [17]. CDDs have also played a valuable role in operational research and national surveillance [14]. For example, the APOC has enlisted CDDs to gather data of value for other programs and studies, such as the latitude and longitude of each village and health center, and the demographic characteristics of households in 32,000 communities [48]. In 2012, over 650,000 CDDs were trained or re-trained in 22 countries, as were over 80,000 health workers in 20 countries [78].

In addition to the benefits of the CDTI system, onchocerciasis control and elimination may contribute to the overall health of affected populations. In sub-Saharan Africa, the same populations affected by HIV, TB and malaria are often polyparasited with NTDs [1]. Research now shows that NTDs render individuals more susceptible to

the “big three,” and that co-infection may worsen outcomes for patients [1,8,68]. In particular, helminth infections are thought to weaken the immune response and may impair the ability to seroconvert after vaccination [23,61].

Treatment with ivermectin also confers secondary benefits [70,71]. While albendazole is now the recommended drug for STHs, ivermectin has a “significant effect” on Ascaris and Trichuris and is the “drug of choice” for human strongyloidiasis [8,17]. MDA has shown a reduction in prevalence of ectoparasitic skin infections such as lice, fleas and scabies, as well as the secondary skin infections they cause [8]. Ivermectin has proved to be a popular drug due to the immediate relief from itching associated with onchocerciasis and other parasites [17]. Affected individuals attest that the drug improves overall social, psychological and economic well-being [54].

MDG 8: Develop a global partnership for development

As a collaboration between the WHO, UN, World Bank, FAO, the pharmaceutical company Merck, 31 African countries, 21 bilateral and multilateral donors, over 20 international and local NGOs, and over 190,000 endemic communities, the APOC is an exemplary illustration of the global partnerships envisioned in MDG 8 [17,78].

Specifically, target 8E states, “in cooperation with pharmaceutical companies, provide access to affordable essential drugs in developing countries” [7]. In 1987, Merck began donating ivermectin for “as long as needed” to help fight river blindness [2]. Merck later extended this donation to include treatment for Lymphatic Filariasis (LF), an NTD which requires treatment with both ivermectin and albendazole (donated by GlaxoSmithKline) [17]. Merck bears the cost of production, transportation to the port of entry and any clearing costs, while the MDP manages administration and distribution of the drugs to the entities responsible for implementation [51]. Merck has calculated the value of each tablet to be $1.50, which would put their donation over the past twenty years at over two billion dollars [51,62].

Merck’s long-term commitment is one of the key reasons for the success of the onchocerciasis programs. It allowed governments and NGOs the time to invest in operational research without the threat of the programs’ end or need to source other funds [17]. The MDP was the first of its kind and paved the way for similar programs. It is the longest running drug donation program and continues to be one of the largest public-private partnerships ever created [17].

Discussion

The MDGs aim is to reduce extreme poverty and ensure equity in fundamental rights [7]. As demonstrated in this paper, onchocerciasis programs support these exact aims. By reducing the prevalence of a stigmatizing and disabling disease, onchocerciasis programs improve the overall health of individuals. In turn, this allows for gains in

worker productivity, gender equity, and education, thus stimulating the development of affected communities.

Despite the crosscutting impact of onchocerciasis and other NTDs on human development, they have been largely under attended to in global health action. Instead, the primary focus of the past decade has been on the three diseases listed in MDG 6 [8,19,20]. A glance at the allocation of funds by global health entities illustrates this disparity: while HIV/AIDS programs received a full 37% of total international development assistance in 2010, NTDs were allocated a mere 0.6% [15]. While these high mortality diseases need to be addressed, current strategies are limited to treatment and containment [8]. The control and elimination of several NTDs that have plagued humanity for centuries, however, is within reach [11].

Looking towards the post-2015 agenda, it is imperative that the global community evaluate past development efforts, and build upon and invest in those that work. Focus on "low hanging fruits" with proven and cost-effective strategies is prudent. Since these poverty-promoting diseases affect nearly one billion people [12], and are thought to worsen the health outcomes of those co-infected with priority diseases, the benefits of NTD control would likely extend beyond disease specific targets. Furthermore, many NTD programs offer opportunities for integrated health delivery. For instance, as discussed, the addition of multiple health interventions to community directed treatment of ivermectin led to increased coverage and decreased operational costs.

Onchocerciasis control is widely considered to be one of the most successful and cost-effective public health campaigns ever launched [2,23]. Its 40-year history provides valuable lessons in disease control, and yielded multiple best practices worth emulating. Among these, efforts to control onchocerciasis highlight the need for good data; mapping of onchocerciasis infection, in combination with rigorous monitoring, allows countries to prioritize treatment areas and ensure adequate coverage. These programs also show the value of strong multilateral partnerships; the organization of onchocerciasis control allows each partner to focus on their specialty while benefiting from the experiences and expertise of a team. Perhaps most pertinent to the global health community, though, is the demonstrated effectiveness of facilitating community ownership, by allowing communities considerable agency with regard to drug delivery. With a network of over 650,000 CDDs throughout 190,000 communities [21], APOC has not only strengthened distribution lines across Africa, but it empowers individuals to take an active role in their health.

While onchocerciasis control is indisputably a major public health achievement, evidence of interrupted transmission in 11 of 13 endemic regions in the Americas and several foci in Africa, raises hopes for a more sustainable solution [43]. Moving towards a goal of elimination, it will be necessary to address the technical challenges of MDA in areas co-endemic with loiasis, as ivermectin can cause severe adverse reactions in co-infected individuals, as well as reaching therapeutic coverage levels in regions with

ongoing conflicts [26]. More research is also urgently needed to develop a safe and effective macrofilaricide to kill adult worms, as well as develop better diagnostic tests [22-24,26]. In the meantime, mathematical models suggest that moving to semi-annual treatment, and vector control where feasible, will drastically reduce the time frame required to interrupt transmission. In sum: though highly efficient vectors and the vast terrain of Africa represent considerable challenges, with adequate resources and the persistence of all involved, movement towards elimination is possible. The right political will and stakeholder commitment to these efforts can make it so that future generations will never know the sufferings once caused by the bite of the black fly.

Table 5: The Impact of Onchocerciasis Control and Elimination Programs on the MDGs

MDG	**Impact of Onchocerciasis**	**Impact of Onchocerciasis Programs and Disease Reduction**
MDG 1: Eradicate extreme poverty and hunger	Agricultural production losses due to migration from fertile lands [22,27]	Vector control programs allow 25 million hectares to be reclaimed, enough food to feed over 18 million [1,22]
	Decreased worker productivity due to severe visual impairment and associated pain and fatigue [1,52]	Treatment with ivermectin reduces morbidities; [22] continuation of productive work [54]
	Affected individuals spent more time and money seeking healthcare; medical poverty trap [27,51,52]	Treatment with ivermectin reduces morbidities; [22] time and money can be redirected
MDG 2: Achieve universal primary education	Children removed from school to care for affected relatives [52]	Reduced prevalence of onchocerciasis in the community; students stay in school [54]
	Severe itching and fatigue affect ability to concentrate and learn [27]	Ivermectin relieves itching from onchocerciasis and reduces ectoparasitic skin infections and certain intestinal parasites; student's ability to focus and learn improved [1,8,17]
MDG 3: Promote gender equality and empower women	Stigma associated with disease prevents women from being married; impacts mental health	Reduced morbidities allow women to participate freely in community life [76]

	[18,29,75]	
	Girls more likely to be removed from school to care for affected relatives [52]	Reduced prevalence of onchocerciasis in the community; girls stay in school [52]
		Recruitment of CDDs; women empowered to effect change within the community
MDG 4: Reduce child mortality	(No known impact)	Reduced morbidities allow women to provide prolonged breastfeeding protection to children [55]
		Reduced prevalence of onchocerciasis in the community; under-five less likely to become infected, improving development outcomes (helminth infection associated with impaired immune response) [57,60,61]
MDG 5: Reduce maternal mortality	(No known impact)	CDDs provide health education, including family planning [78]
MDG 6: Combat HIV/AIDS, malaria, and other diseases	Onchocerciasis as a disease; second leading infectious cause of blindness in the world; morbidities include OSD, hanging groin, weight loss, musculoskeletal pain, insomnia and fatigue [1,27,52]	CDTI and vector control strategies; reduced prevalence of onchocerciasis in the community
	Helminth infections impairs immune response and ability to seroconvert after vaccination; co-infection with NTDs and "big three" may worsen outcomes for patients [1,8,23,61,68]	Ivermectin reduces helminth burden [70,71]
		CDTI system facilitates integration with other health programs; improved coverage and uptake of services; cost savings [64-66,68,69,78]

		Strengthens health systems through operational research, training of CDDs and health workers and expanded distribution lines [8,17,48,62,63,78]
		Treatment with ivermectin confers secondary benefits; effective against certain intestinal parasites and ectoparasitic skin infections [1,8,17]
MDG 7: Ensuring environmental sustainability	(No known impact)	Vector control areas make use of environmentally safe larvicides; MDG is not impeded
MDG 8: Develop a global partnership for development	(No known impact)	Increased access to the drug, ivermectin, through drug donation by Merck [51,62]
		MDP is one of the largest public-private partnerships ever created; first of its kind and paved the way for similar programs. [17,78]

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CHAPTER IV: CONCLUSIONS AND RECOMMENDATIONS

Discussion

History bears witness to the devastation once inflicted on individuals and communities by onchocerciasis. Forty years ago, the images of deserted villages and children leading the blind with sticks were commonplace in the hyper-endemic regions of West Africa; and before the discovery of ivermectin, the disease plagued affected individuals with its telltale symptoms of de-pigmented, rough skin, along with its maddening itch. Yet, thanks to an extensive global partnership, efforts to control and eliminate onchocerciasis have proved it is not only possible to relieve physical suffering, but that the benefits of ridding communities of this burden extend beyond health, to nearly all aspects of people's lives.

The crosscutting impact of these programs aligns with nearly all of the MDGs. Decades of research have shown the impact of onchocerciasis on human development and the effectiveness of control and elimination programs. With improved health and reclaimed fertile lands, farmers' productivity and agricultural yields are increased, thus decreasing poverty and hunger (MDG 1 and 4). As the prevalence of blindness dissipates, so too, does the number of students (particularly girl children) who must leave school to care for their disabled relatives (MDG 2 and 3). These children are more capable of learning, as relief from constant and unbearable itching allows them to be well rested and focus in school (MDG 2). In treating affected individuals, most of the visible symptoms of onchocerciasis are reduced, freeing individuals from the stigma associated with OSD and constant scratching; this is particularly beneficial to women whose suitability for marriage, and thus economic security, is affected by the disease (MDG 3). With this reduction in skin disease, women are also more likely to continue breastfeeding,

extending health benefits to their babies (MDG 4). Moreover, treatment with ivermectin bestows secondary health benefits such as a reduction in ectoparasitic skin infections and certain intestinal helminthes. Not only does this improve the general wellbeing those affected, but it may also have an indirect impact on high mortality diseases as helminth infections are thought to weaken immune response (MDG 6). Years of operational research have elicited best practices in public health, provided surveillance information and strengthened distribution lines (MDG 6). Lastly, the MDP, one of the largest and longest-running public-private partnerships ever launched, has provided access to treatment for millions of individuals and paved the way for similar drug donation programs (MDG 8).

With this said, it is not possible to quantify the contribution of these programs towards the achievement of MDGs; since each use different indicators to measure progress, it is only possible to demonstrate an association (See Table 5). Available data was explored to see if any correlation exists between levels of therapeutic coverage and MDG progress. The results are shown below:

Figure 3: APOC Country Progress by 2012 Therapeutic Coverage

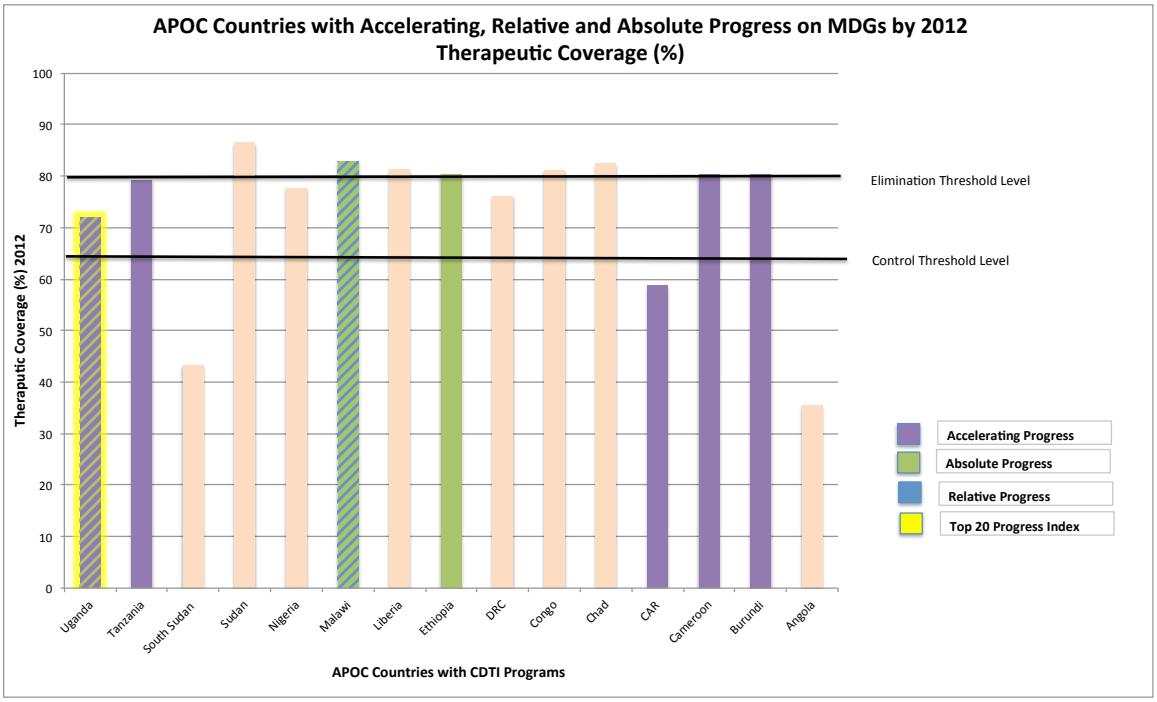
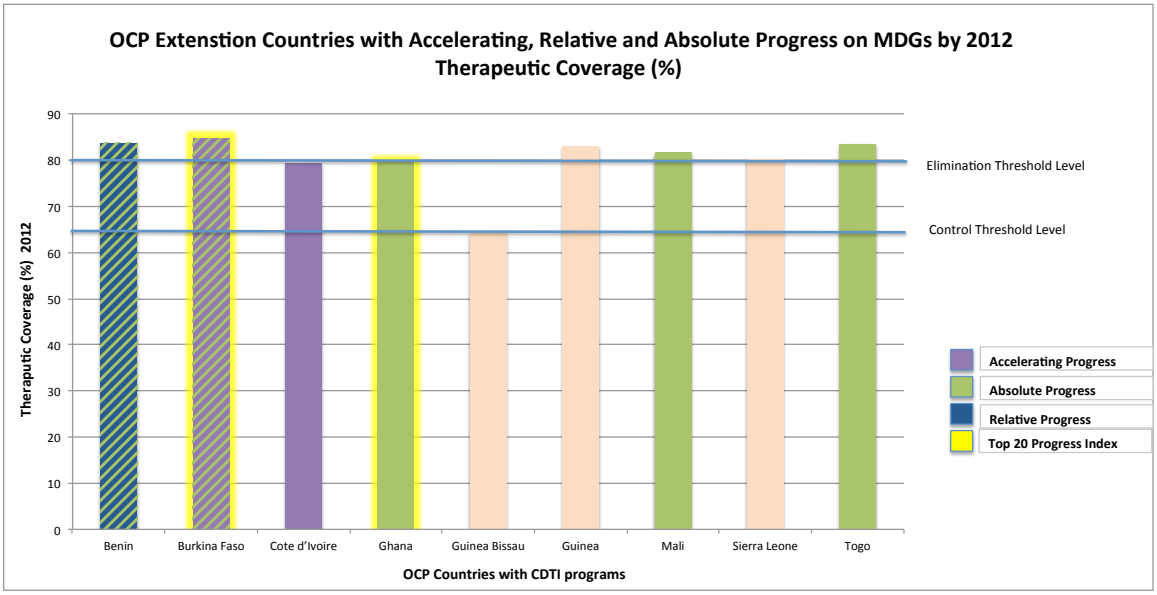


Figure 4: OCP Country Progress by 2012 Therapeutic Coverage



No pattern can be seen; some countries that achieved high coverage levels still had poor development outcomes, while several countries with low coverage are doing relatively well in terms of MDG progress. Had a pattern emerged, it would not have indicated a correlation between onchocerciasis control and national progress, but rather a proxy for other factors such as the strength of health systems. Given this notion, it might be expected that countries highlighted for their development progress would also have higher levels of therapeutic coverage. However, these figures illustrate that the effectiveness of onchocerciasis programs and MDG progress have no relation to one another. As a vertical program, onchocerciasis programs are able to meet their targets, despite challenges such as low levels of development; however, the impact of such programs does not extend to national progress. It should be noted that, in addition to challenges with measuring MDG progress, these graphs are limited because they do not reflect burden of disease for each country, nor do they indicate historic treatment trends. (Further details on country progress are provided in the appendix).

Even though it is not reflected in national progress measures, there is no question that onchocerciasis programs have made a significant impact on affected communities. Onchocerciasis control is widely considered to be one of the most successful and cost-effective public health campaigns ever launched [2,23]. The reach of these programs is enormous. The OCP is credited with preventing the infection of some 40 million people, preventing blindness of 600,000, and allowing 25 million hectares of land to be reclaimed in West Africa [2,17]. APOC is estimated to have prevented the loss of 8.2 million DALYs between 1995-2010, and is projected to double this number, averting 9.2 additional DALYs, by 2015 [79]. Moreover, since onchocerciasis is primarily found “at

the end of the road," in the poorest of poor communities, these programs undoubtedly impact the very population that the MDGs were intended to benefit.

Despite their clear "pro-poor" impact, onchocerciasis and other NTDs were not explicitly mentioned in the MDGs. The reason this matters is funding. While, in recent years, there has been more attention and resources directed to NTD programs, it still pails in comparison to that which is allocated to the "big three" named in MDG 6 [15]. There is little dispute that the MDGs have served to frame the development agenda and were an impetus for increased development assistance [74]. While the 1990s saw a period of stagnation for aid, the new millennium ushered in a significant increase in ODA; from $72 billion in 2000, to $128 billion in 2009. These numbers are in line with the time frame and projected cost to achieve the MDGs, suggesting a causal link [72]. However, the MDGs also seem to have prompted a trend of sector based funding around priority health areas; the largest of these are notably the Global Alliance for Vaccines and Immunizations (GAVI) and the President's Emergency Plan For AIDS Relief (PEPFAR). Though overall levels of ODA rose significantly, resources were funneled into priority sectors [72]. A glance at the allocation of funds by global health entities illustrates this disparity: while HIV/AIDS programs received a full 37% of total international development assistance in 2010, NTDs received a mere 0.6% [15].

Despite this increase in funding, in many countries, aid hasn't resulted in desired outcomes. While there are numerous explanations for the low return on investment, one is simply that the goals are too lofty [74]. Progress is being made, but without accelerated economic development and strengthened health systems, it is unlikely most of the low-income countries will meet the goals in time. Another challenge is that high mortality

causing diseases, such as HIV/AIDS and malaria don't have effective (or at-least cost-effective) control strategies and are limited to treatment and containment [8].

NTDs, on the other hand, which affect nearly one billion people and are thought to worsen the health outcomes of those co-infected with these priority diseases, have proven and cost-effective control strategies. NTD control also offers opportunities for integration; combining health interventions with CDTI for onchocerciasis has been shown to increase coverage for multiple other health programs, and in the process, cut operational costs. CDTI also provides a point of intervention for hard to reach individuals, such as those in remote or conflict-affected areas. Given this context, the global health community should focus on such "low hanging fruits" that have existing and efficacious strategies. Reducing disability and stigma caused by onchocerciasis and other NTDs will improve the overall wellbeing of poor populations and provide a "leg up" to tackle some of these more complex problems.

The Way Forward

While onchocerciasis control is indisputably a major public health achievement, evidence of interrupted transmission in 11 of 13 endemic regions in the Americas and several foci in Africa, raises hopes for a more sustainable solution [43]. Given these and other successes, the APOC will officially shift from a mission of control to elimination in 2016. In addition, the program will attempt to integrate NTD programs where there is geographic overlap and complementary treatment protocol. The initial expansion will focus on lymphatic filariasis (LF), a helminth disease spread by mosquitos, which leads to lymphedema and elephantiasis. LF can be treated with a combination of albendazole

and ivermectin, making it a good candidate for integrated drug delivery through the CDD network [30,44,80].

Moving towards this goal of elimination, it will be necessary to address the technical challenges of MDA in areas co-endemic with loiasis, as ivermectin can cause severe adverse reactions in co-infected individuals, as well as reaching therapeutic coverage levels in regions with ongoing conflicts [26]. More research is urgently needed to develop a safe and effective macrofilaricide to kill adult worms, as well as develop better diagnostic tests [22-24,26]. Research should also be encouraged to understand the impact of onchocerciasis on other diseases, including some mysterious conditions, such as Nkalanga Syndrome and a specific type of epilepsy known as Nodding Syndrome.
In the meantime, mathematical models suggest that moving to semi-annual treatment, and vector control where feasible, will drastically reduce the time frame required to interrupt transmission of onchocerciasis [42,81].

Public Health Implications

Onchocerciasis control and elimination programs have a well-documented history of success that offers invaluable lessons and best practice in public health. Chiefly, they are data-driven; this allows for program prioritization and progress to be measured on a regular basis, so that necessary modifications can be made. Additionally, the strong global partnership that exists has led to extensive operational research and collaboration among stakeholders. Perhaps most pertinent to the global health community is that programs have moved towards community ownership, by allowing communities to choose when and how drug delivery happens. With a network of over 650,000 CDDs throughout 190,000 communities, the program has not only strengthened distribution

lines, but also empowered individuals to take an active role in their health [21]. This willingness of communities to self-organize and take collective action should be tapped into and built upon by other development programs.

Despite the broad impact of onchocerciasis on human development demonstrated in this thesis, little recent research points to the utility of NTD programs in relation to the MDGs. The author of this paper hopes to draw the attention of public policymakers and global health funders to the role onchocerciasis and other NTDs play in hindering development, and advocate for their inclusion in the post-2015 agenda. While, in recent years, there has been greater recognition of the poverty promoting attributes of NTDs, as well as the possibilities for cost savings through integrated NTD control, this has come from a limited group. Recognition within the UN post-2015 agenda would contribute to broader recognition and support among global health entities, which, in turn, may help fuel the drive towards elimination.

REFERENCES

1. Norris J, Adelman C, Spantchak Y, Marano K (2012) Social and Economic Impact Review on Neglected Tropical Diseases Washington, DC: The Hudson Institute. 36 p.
2. Crump A, Morel CM, Omura S (2012) The Onchocerciasis Chronicle: From the Beginning to the End? Trends in Parasitology 28: 9.
3. Attaran A (2005) An immeasurable crisis? A criticism of the millennium development goals and why they cannot be measured. PLoS Med 2: e318.
4. Leo B, Thuotte R, Bartram J, Elliott M, Chuang P, et al. (2012) MDG Progress Index 2011. The good (country progress) the bad (slippage) and the ugly (fickle data). Lancet 380: 85-86.
5. Friedman HS (2013) Causal Inference and the Millennium Development Goals (MDGs): Assessing Whether There Was an Acceleration in MDG Development Indicators Following the MDG Declaration.
6. Haines A, Cassels A (2004) Can the millennium development goals be attained? BMJ 329: 4.
7. United Nations (2000) 55/2. United Nations Millennium Declaration New York United Nations.
8. Molyneux DH, Hotez PJ, Fenwick A (2005) "Rapid-Impact Interventions": How a Policy of Integrated Control for Africa's Neglected Tropical Diseases Could Benefit the Poor. PLoS Mediciine 2: 7.
9. Beaglehole R, Bonita R (2008) Global Public Health: A Scorecard. The Lancet 372: 9.
10. United Nations Economic Commission for Africa (2013) MDG Report 2013: Assessing Progress in Africa toward the Millennium Development Goals.
11. Hotez P, Ottesen E, Fenwick A, Molyneux D (2006) The Neglected Tropical Diseases: The Ancient Afflictions of Stigma and Poverty and the Prospects for their Control and Elimination. In: Pollard AJ, Finn A, editors. Hot Topics in Infection and Immunity in Children. New York: Springer. pp. 11.
12. World Health Organization (2009) Neglected tropical diseases, hidden successes, emerging opportunities. In: Diseases DoCoNT, editor.
13. Conteh L, Engels T, Molyneux DH (2010) Socioeconomic Aspects of Neglected Tropical Diseases. The Lancet 375: 9.
14. Hotez PJ, Fenwick A, Savioli L, Molyneux DH (2009) Rescuing the Bottom Billion Through Control of Neglected Tropical Diseases The Lancet 373: 6.
15. Kirby T (2010) David Molyneux: raising the profile of neglected tropical diseases. The Lancet 375: 21.
16. Harris M, Reza J (2012) Global report for research on infectious diseases of poverty: World Health Organization.
17. Levine R (2004) Millions saved: proven successes in global health: Peterson Institute.
18. World Health Organization (2013) Sustaining the drive to overcome the global impact of neglected tropical diseases. Geneva, Switzerland.
19. Feasey N, Wansbrough-Jones M, Mabey DCW, Solomon AW (2009) Neglected Tropical Diseases. British Medical Bulletin 93: 22.
20. Molyneux DH (2010) Neglected Tropical Diseases—Beyond the Tipping Point? The Lancet 375: 2.

21. World Health Organization (2013) African Programme for Onchocerciasis Control: meeting of national onchocerciasis task forces, September 2013. Weekly epidemiological record.
22. Uche Amazigo MN, Jesse Bump, Bruce Benton, Bernhard Liese, Laurent Yameogo, Honorat Zoure, Azodoga Seketeli (2006) Onchocerciasis In: Jamison DT FR, Makgoba MW, et al., editor. Disease and Mortality in Sub-Saharn Africa. 2nd edition ed. Washington, DC: World Bank.
23. Basáñez M-G, Pion SDS, Churcher TS, Breitling LP, Little MP, et al. (2006) River Blindness: A Success Story Under Threat? PLos Medicine 3: 7.
24. Boatin BA, Richards Jr FO (2006) Control of onchocerciasis. Advances in parasitology 61: 349-394.
25. Kale OO (1997) Onchocerciasis: the Burden of Disease. Annals of Tropical Medicine & Parasitology 92: 15.
26. Hopkins A (2005) Ivermectin and Onchocerciasis: Is It All Solved? Eye 19: 10.
27. Ubachukwu PO (2006) Socio-Economic Impact of Onchocerciasis with Particular reference to Females and Children: A review Animal Research International 3: 11.
28. World Health Organization (2001) Certification of Elimination of Human Onchocerciasis: Criteria and Procedures. World Health Organization. 36 p.
29. National Research Council (1996) In her lifetime: female morbidity and mortality in sub-Saharan Africa: The National Academies Press.
30. Hoerauf A, Pfarr K, Mand S, Debrah AY, Specht S (2011) Filariasis in Africa—treatment challenges and prospects. Clinical Microbiology and Infection 17: 9.
31. Landau E (2013) With river blindness, 'you never sleep'. CNN.
32. Browne SG (1976) Onchocerciasis and the Skin. African Medical Journal 50: 4.
33. Elizabeth Litt MCB, David Molyneux (2012) Neglected Tropical Diseases and Mental Health: a Perspective on Comorbidity Trends in Parasitology 28: 7.
34. Nelson GS (1958) "Hanging Groin" and hernia, Complications of Onchocerciasis. Transactions of the Royal Society of Tropical Medicine and Hygiene 52: 4.
35. Vlassoff C (1994) Gender Inequalities in Health in The Third World: Uncharted Ground. Social Science and medicine 39: 11.
36. Newell ED, Vyungimanal F, Bradley JE (1991) Epilepsy, Retarded Growth and Onchocerciasis, in Two Areas of Different Endemicity of Onchocerciasis in Burundi Transactions of the Royal Society of Tropical Medicine and Hygiene 97: 3.
37. Kaiser C, Pion S, Boussinesq M (2010) Do helminths cause epilepsy? The case of Onchocerca volvulus. Parasite immunology 32: 79-80.
38. Guderian RH, Lovato R, Ansehni M, Mancero T, Cooper PJ (1997) Onchocerciasis and Reproductive Health in Ecuador. Transactions of the Royal Society of Tropical Medicine and Hygiene 91: 3.
39. Alonso LM, Murdoch ME, Jofre-Bonet M (2009) Psycho-social and Economic Evaluation of Onchocerciasis: a Literature Review Social Medicine 4: 24.
40. Hotez PJ (2008) Stigma: The Stealth Weapon of the NTD. PLoS Neglected Tropical Diseases 2: 2.
41. Weiss MG (2008) Stigma and the Social Burden of Neglected Tropical Diseases PLoS Neglected Tropical Diseases 2: 6.

42. Cupp EW, Cupp MS (2005) Short report: impact of ivermectin community-level treatments on elimination of adult Onchocerca volvulus when individuals receive multiple treatments per year. Am J Trop Med Hyg 73: 1159-1161.
43. The Carter Center (2014) River Blindness Elimination Program
44. World Health Organization (2014) African Program for Onchocerciasis Control (APOC)
45. Bump JB, Benton B, Seketeli A, Liese BH, Novinskey C (2006) Defeating Riverblindness Thirty Years of Success in Africa. Attacking Africa's Poverty: Experience from the Ground. pp. 285-318.
46. Thylefors B (2004) Eliminating onchocerciasis as a public health problem. Tropical Medicine and International Health 9: 3.
47. Blanks J, Richards F, Beltran F, Collins R, Alvarez E, et al. (1998) The Onchocerciasis Elimination Program for the Americas: a history of partnership. Revista Panamericana de Salud Pública 3: 367-374.
48. Amazigo U (2008) The African Programme for Onchocerciasis Control (APOC) Annals of Tropical Medicine & Parasitology 102: 4.
49. Colatrella B (2008) The Mectizan Donation Program: 20 years of successful collaboration - a retrospective. Ann Trop Med Parasitol 102 Suppl 1: 7-11.
50. Gustavsen K, Hopkins A, Sauerbrey M (2011) Onchocerciasis in the Americas: from arrival to (near) elimination. Parasit Vectors 4: 205.
51. Waters HR, Rehwinkel JA, Burnham G (2004) Economic evaluation of Mectizan distribution. Tropical Medicine and International Health 9: 10.
52. Benton B (1998) Economic Impact of Onchocerciasis Control Through the African Programme for Onchocerciasis Control: an Overview. Annals of Tropical Medicine & Parasitology 92: 8.
53. Evans T (1989) The Impact of Permanent Disability on Rural Households: River Blindness in Guinea. IDS Bulliten 20: 10.
54. Okeibunor JC, Amuyunzu-Nyamongo M, Onyeneho NG, Tchounkeu YFL, Manianga C, et al. (2011) Where Bould I Be Without Ivermectin? Capturing the Benefits of Community-directed Treatment with Ivermectin in Africa Tropical Medicine and International Health 16: 14.
55. Amazigo UO (1994) Detrimental Effects of Onchocerciasis on Marriage Age and Breast feeding. Tropical and Geographical medicine 46: 5.
56. Amazigo U (1993) Onchocerciasis and Women's Reproductive Health. Tropical Doctor 23: 3.
57. Walker M, Little MP, Wagner KS, Soumbey-Alley EW, Boatin BA, et al. (2012) Density-Dependent Mortality of the Human Host in Onchocerciasis: Relationships between Microfilarial Load and Excess Mortality PLoS Neglected Tropical Diseases 6: 13.
58. Soboslay PT, Geiger SM, Drabner B, Banla M, Batchassi E, et al. (1999) Prenatal Immune Priming in Onchocerciasis—Onchocerca volvulus-specific Cellular Responsiveness and Cytokine Production in Newborns from Infected mothers Clinical and Experimental Immunology 117: 8.
59. Nwaorgu OC, Okeibunor JC (1999) Onchocerciasis in Pre-primary School Children in Nigeria: Lessons for Onchocerciasis Country Control Programme Acta Tropica 73: 5.

60. Hotez PJ, Brindley PJ, Bethony JM, King CH, Pearce EJ, et al. (2008) Helminth Infections: the Great Neglected Tropical Diseases. The Journal of Clinical Investigation 118: 11.
61. Stewart G, Boussinesq M, Coulson T, Elson L, Nutman T, et al. (1999) Onchocerciasis modulates the immune response to mycobacterial antigens. Clinical and experimental immunology 117: 517.
62. Haddad D, Cross C, Thylefors B, Richards Jr F, Bush S, et al. (2008) Health care at the end of the road: opportunities from 20 years of partnership in onchocerciasis control. Global Public Health 3: 187-196.
63. Seketeli A, Adeoye G, Eyamba A, Nnoruka E, Drameh P, et al. (2002) The achievements and challenges of the African Programme for Onchocerciasis Control (APOC). Annals of tropical medicine and parasitology 96: 15-28.
64. Katabarwa MN, Habomugisha P, Richards Jr FO, Hopkins D (2005) Community-Directed Interventions Strategy Enhances Efficient and Effective Integration of Health Care Delivery and Development Activities in Rural Disadvantaged Communities of Uganda Tropical Medicine and International Health 10: 10.
65. Okeibunor JC, Ogungbemi MK, Sama M, Gbeleou SC, Oyene U, et al. (2008) Additional health and development activities for community-directed distributors of ivermectin: threat or opportunity for onchocerciasis control? . Tropical Medicine and International Health 9: 10.
66. World Health Organization (2008) Community Directed Interventions for Major Health Problems in Africa Switzerland.
67. Katabarwa MN, Habomugisha P, Agunyo S, McKelvey AC, Ogweng N, et al. (2010) Traditional Kinship System Enhanced Classic Community-directed Treatment with Ivermectin (CDTI) for Onchocerciasis Control in Uganda Transactions of the Royal Society of Tropical Medicine and Hygiene 104: 8.
68. Hotez PJ, Molyneux, David H., Fenwick A, Ottesen E, Sachs SE, et al. (2006) Incorporating a Rapid-Impact Package for Neglected Tropical Diseases with Programs for HIV/AIDS, Tuberculosis, and Malaria. PLos Medicine 3: 9.
69. Brady MA, Hooper PJ, Ottesen EA (2006) Projected Benefits from Integrating NTD Programs in Sub-Saharan Africa Trends in Parasitology 22: 7.
70. Gutman J, Emukah E, Okpala N, Okoro C, Obasi A, et al. (2010) Effects of Annual Mass Treatment with Ivermectin for Onchocerciasis on the Prevalence of Intestinal Helminths. The American Journal of Tropical Medicine and Hygiene 83: 8.
71. Moncayo AL, Vaca M, Amorim L, Rodriguez A, Erazo S, et al. (2008) Impact of Long-Term Treatment with Ivermectin on the Prevalence and Intensity of Soil-Transmitted Helminth Infections PLoS Neglected Tropical Diseases 2: 9.
72. Kenny C, Sumner A (2011) More money or more development: what have the MDGs achieved. Center for Global Development working paper 278.
73. United Nations Statistics Division Millennium Development Goals Indicators: The official United Nations site for the MDG Indicators.
74. Leo B, Barmeier J (2010) Who are the MDG trailblazers? a new MDG progress index. Center for Global Development Working Paper 222.
75. Litt E, Baker MC, Molyneux D (2012) Neglected tropical diseases and mental health: a perspective on comorbidity. Trends in parasitology 28: 195-201.

76. Vlassoff C, Weiss M, Ovuga E, Eneanya C, Nwel PT, et al. (2000) Gender and the stigma of onchocercal skin disease in Africa. Social science & medicine 50: 1353-1368.
77. Amazigo U (1993) Onchocerciasis and women's reproductive health: indigenous and biomedical concepts. Tropical doctor 23: 149-151.
78. World health Organization (2012) African Programme for Onchocerciasis Control: meeting of national onchocerciasis task forces, September 2012. Weekly epidemiological record.
79. Coffeng LE, Stolk WA, Zoure´ HGM, Veerman JL, Agblewonu KB, et al. (2013) African Programme for Onchocerciasis Control 1995–2015: Model-Estimated Health Impact and Cost PLoS Neglected Tropical Diseases 7: 9.
80. Taylor MJ, Hoerauf A, Bockarie M (2010) Lymphatic filariasis and onchocerciasis. Lancet 376: 1175-1185.
81. Cupp E, Sauerbrey M, Richards F (2011) Elimination of human onchocerciasis: History of progress and current feasibility using ivermectin (Mectizan< sup>®</sup>) monotherapy. Acta tropica 120: S100-S108.
82. King CH, Bertino A-M (2008) Asymmetries of poverty: why global burden of disease valuations underestimate the burden of neglected tropical diseases. PLoS neglected tropical diseases 2: e209.

APPENDICES

DALYS

Disability Adjusted Life Years (DALYS) are an international standard for measuring and comparing the burden of various diseases. These calculations are age-adjusted and express the years of healthy life lost from premature death and disability. One DALY represents one year of healthy life lost [1].

DALY calculations are limited in application to NTDs for a number of reasons, not the least of which is that it is impossible to parse out the burden attributed to each disease, particularly in areas in which people are polyparasitized and suffer from multiple ailments. This is particularly difficult when syndromes are involved. For instance several NTDs are through to exacerbate anemia and malnutrition, yet the DALY system does not allow for these disabilities to be shared, so the symptoms are given their own disability weight rather being attributed to an underlying cause [82].

DALYs are considered underestimated for NTDs for several other reasons [82]. When DALYs are calculated, mortality is given a larger weighting than morbidity so the burden of NTDs appear less in comparison to diseases that shorten life expectancy, although living with serve disability may be considered worse to affected individuals. For instance, research shows that NTDs impose costly social and psychological burdens upon affected individuals [33]. Disability weights were awarded to diseases based on the consensus of non-expert, highly educated panels using a “person trade-off” method during the late 1980s and early 1990s. This economic approach was intended to result in a subjective analysis, but some argue the weights are from a Western perspective that

ignores the realities of the patients affected. NTDs primarily affect people living in poverty. As such, the experiences of living with a disability are very different from an affluent context [13,82]. For example, the support systems in place for blind persons in England differ greatly from those in rural Zambia. The system of age weighting is also problematic for its cultural variation. In the calculations of DALYS, children and elderly are given a lower disability weight than those of middle age who are considered productive. Yet, in many cultures, particularly in impoverished communities, children and elderly make significant contributions to household productivity [82].

Table 6: MDG Progress of Onchocerciasis Affected Countries

OCP

Country	**MDG Progress**	**Top Performers**	**CGD Progress Index Score (out of 8.0)**
Benin	1. Off track 2. Possible 3. Possible 4. Insufficient data 5. Off track 6. Possible 7. Insufficient data 8. Insufficient data	2010 Absolute Progress 2010 Relative Progress	4.0
Burkina Faso	1. Insufficient data 2. Possible 3. Possible 4. Off track 5. Possible 6. Possible 7. Possible 8. Insufficient data	2010 Absolute Progress 2011 Top 20 Overall 2012 Top 20 Accelerating	5.5
Cote d'Ivoire	1. Insufficient data 2. Off track 3. Off track 4. Possible 5. Possible 6. Possible 7. Possible 8. Insufficient data	2012 Top 20 Accelerating	0.0
Ghana	1. Insufficient data 2. Possible 3. Off track 4. Off track 5. Off track 6. Off track 7. Possible 8. Possible	2010 Top 20 absolute progress 2011 Top 20 Overall	5.0
Guinea Bissau	1. Insufficient data 2. On track 3. On track 4. Possible 5. Possible 6. Possible 7. Possible 8. Insufficient data		0.5
Guinea	1. Off track 2. Possible 3. Off track 4. Possible 5. Possible 6. Possible 7. Possible 8. Insufficient data		3.5
Mali	1. Possible 2. Possible 3. Possible 4. Possible 5. Off track 6. Possible 7. Insufficient data 8. Insufficient data	2010 Absolute Progress	4.5
Niger	1. Off track 2. Off track 3. Off track		4.0

	4. On track 5. Off track 6. On track 7. Off track 8. Insufficient data		
Senegal	1. Possible 2. On track 3. Possible 4. On track 5. Off track 6. Possible 7. Possible 8. Possible		3.5
Sierra Leone	1. Possible 2. On track 3. On track 4. Possible 5. Possible 6. On track 7. Off track 8. Insufficient data		2.0
Togo	1. Insufficient info 2. Possible 3. Off track 4. Off track 5. Off track 6. Possible 7. Insufficient data 8. Insufficient data	2010 Absolute Progress	3.0

APOC

Country	**MDG Progress**	**Top Performers**	**CGD Progress Index Score (out of 8.0)**
Angola	1. Off track 2. On track 3. On track 4. Possible 5. Possible 6. Possible 7. Possible 8. Insufficient data		2.5
Burundi	Not included	2012 Top 20 Accelerating	1.5
Cameroon	1. Insufficient data 2. On track 3. Off track 4. Off track 5. Off track 6. Possible 7. Insufficient data 8. Insufficient data	2012 Top 20 Accelerating	3.5
Central African Republic	1. Off track 2. Possible 3. Possible 4. Possible 5. Off track 6. Possible 7. Possible 8. Insufficient data	2012 Top 20 Accelerating	1.0
Chad	1. Insufficient data 2. On track 3. Off track 4. Off track 5. Off track		2.0

	6. Off track 7. Off track 8. Insufficient data		
Congo	1. Insufficient data 2. On track 3. Off track 4. Possible 5. Possible 6. Insufficient data 7. Possible 8. Insufficient data		2.5
Democratic Republic of Congo	1- Insufficient data 2- Off track 3-Possible 4-Off track 5-Off track 6-Possible 7-Possible 8-Insufficient data		0.0
Ethiopia	1. Possible 2. On track 3. On track 4. On track 5. On track 6. On track 7. On track 8. Possible	Absolute Progress 2010	4.5
Equatorial Guinea	1. Insufficient data 2. On track 3. Possible 4. On track 5. On track 6. On track 7. Possible 8. Insufficient data		Not listed
Gabon	1. On track 2. On track 3. On track 4. On track 5. On track 6. Insufficient data 7. Possible 8. Insufficient data		1.5
Kenya	1. Off track 2. On track 3. Possible 4. Possible 5. Possible 6. Possible 7. Possible 8. Insufficient data	2012 Top 20 Accelerating	1.5
Liberia	1. Off track 2. Possible 3. Possible 4. Possible 5. Possible 6. Possible 7. Possible 8. Insufficient data		1.5
Malawi	1. Off track 2. Possible 3. Possible 4. Possible 5. Off track 6. Possible 7. Off track 8. Insufficient data	2010 Absolute progress 2010 Relative Progress	4.5
Mozambique	1. Possible 2. Off track	2012 Top 20 Accelerating	3.5

	3. Off track 4. On track 5. On track 6. Off track 7. Off track 8. Insufficient data		
Nigeria	1. Off track 2. On track 3. Possible 4. Off track 5. Off track 6. Possible 7. Insufficient data 8. Insufficient data		2.5
Rwanda	1. On track 2. Insufficient data 3. On track 4. On track 5. On track 6. On track 7. On track 8. Insufficient data	2010 Absolute Progress 2012 Top 20 Accelerating	3.5
Sudan	1. Insufficient data 2. Possible 3. Possible 4. Possible 5. Insufficient data 6. Insufficient data 7. Insufficient data 8. Insufficient data		2.5
South Sudan	No data available		N/A
Tanzania	1. Insufficient data 2. Possible 3. Possible 4. Possible 5. Off track 6. On track 7. Possible 8. Insufficient data	2012 Top 20 Accelerating Performers	1.5
Uganda	1. On track 2. On track 3. On track 4. Off track 5. Off track 6. Possible 7. Possible 8. Insufficient data	2010 Absolute Progress 2011 Top 20 Overall 2012 Top 20 Accelerating	5.0

OEPA

Country	**MDG Progress**	**Top Performers**	**CGD Progress Index Score (out of 8.0)**
Brazil	1. Absolute progress 2. Absolute progress 3. Absolute progress 4. On track 5. On track 6. Absolute progress 7. On track 8. On track	2010 Relative Progress 2011 Top 20 Performers overall	6.5
Colombia	1. Insufficient data 2. Achieved 3. Insufficient data		4.5

	4. On track 5. On track 6. Insufficient data 7. Insufficient data 8. Insufficient data		
Ecuador	1. Possible 2. Possible 3. Possible 4. Possible 5. On track 6. Possible 7. Insufficient data 8. Insufficient data	2010 Relative Progress 2011 Top 20 Overall	7.0
Guatemala	1. Possible 2. Possible 3. Insufficient data 4. Possible 5. Off track 6. Insufficient data 7. Insufficient data	2010 Absolute Progress 2010 Relative Progress	3.5
Mexico	1. On track 2. Achieved 3. On track 4. Achieved 5. Possible 6. On track 7. On track 8. Insufficient data	2010 Relative progress 2011 Top 20 Overall	6.5
Venezuela	1. Insufficient data 2. On track 3. On track 4. On track 5. Possible 6. Possible 7. On track 8. Insufficient data		4.5

Table 7: MDG Goals, Targets and Indicators

Goal 1: Eradicate extreme poverty and hunger	
Target 1.A: Halve, between 1990 and 2015, the proportion of people whose income is less than one dollar a day	1.1 Proportion of population below $1 (PPP) per day 1.2 Poverty gap ratio 1.3 Share of poorest quintile in national consumption
Target 1.B: Achieve full and productive employment and decent work for all, including women and young people	1.4 Growth rate of GDP per person employed 1.5 Employment-to-population ratio 1.6 Proportion of employed people living below $1 (PPP) per day 1.7 Proportion of own-account and contributing family workers in total employment
Target 1.C: Halve, between 1990 and 2015, the proportion of people who suffer from hunger	1.8 Prevalence of underweight children under-five years of age 1.9 Proportion of population below minimum level of dietary energy consumption
Goal 2: Achieve universal primary education	
Target 2.A: Ensure that, by 2015, children everywhere, boys and girls alike, will be able to complete a full course of primary schooling	2.1 Net enrollment ration in primary education 2.2 Proportion of pupils starting grade 1 who reach last grade of primary 2.3 Literacy rate of 15-24 year-olds, women and men
Goal 3: Promote gender equality and empower women	
Target 3.A. Eliminate gender disparity in primary and secondary education, preferably by 2005, and in all levels of education no later than 2015	3.1 Ratios of girls to boys in primary, secondary and tertiary education 3.2 Share of women in wage employment in the non-agricultural sector 3.3 Proportion of seats held by women in national parliament
Goal 4: Reduce child mortality	
Target 4.A: Reduce by two-thirds, between 1990 and 2015, the under-five mortality rate	4.1 Under-five mortality rate 4.2 Infant mortality rate 4.3 Proportion of 1 year-old children immunized against measles
Goal 5: Improve Maternal Health	
Target 5.A: Reduce by three-quarters, between 1990 and 2015, the maternal mortality ratio	5.1 Maternal mortality ratio 5.2 Proportion of births attended by skilled health personnel
Target 5.B: Achieve, by 2015, universal access to reproductive health	5.3 Contraceptive prevalence ratio 5.4 Adolescent birth rate 5.5. Antenatal care coverage (at least one visit and at least four visits) 5.6 Unmet need for family planning
Goal 6: Combat HIV, AIDS, malaria and other diseases	
Target 6.A: Have halted by 2015 and begun to reverse the spread of HIV/AIDS	6.1 HIV prevalence among population aged 15-24 years 6.2 Condom use at last high-risk sex 6.3 Proportion of population aged 15-24 years with comprehensive correct knowledge of HIV/AIDS 6.4 Ratio of school attendance of orphans to school attendance of non-orphans aged 10-14 years
6.B: Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it	6.5 Proportion of population with advanced HIV infection with access to anti-retroviral drugs
6.C: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases	6.6 Incidence of death rates associated with malaria 6.7 Proportion of children under 5 sleeping under insecticide-treated bednets 6.8 Proportion of children under 5 with fever who are treated with appropriate anti-malarial drugs 6.9 Incidence, prevalence and death rates associated with tuberculosis 6.10 Proportion of TB cases detected and cured under directly observed treatment short course.

Goal 7: Ensure environmental sustainability	
Target 7.A: Integrate the principles of sustainable development into country policies and programmes and reverse the loss of environmental resources Target 7.B: Reduce biodiversity loss, achieving, by 2010, a significant reduction in the rate of loss	7.1 Proportion of land area covered by forest 7.2 CO2 Emissions, total, per capita and per $1 GDP (PPP) 7.3 Consumption of ozone-depleting substances 7.4 Proportion of fish stocks within safe biological limits 7.5 Proportion of total water resources used 7.6 Proportion of terrestrial and marine areas protected 7.7 Proportion of species threatened with extinction
Target 7.C: Halve, by 2015, the proportion of people without sustainable access to safe drinking water and basic sanitation	7.8 Proportion of population using an improved drinking water source 7.9 Proportion of population using an improved sanitation facility
Target 7.D: By 2020, to have achieved a significant improvement in the lives of at least 100 million slum dwellers	7.10 Proportion of urban population living in slums
Goal 8: Develop a global partnership for development	
Target 8.A: Develop further an open, rule-based, predictable, non-discriminatory trading and financial system Includes a commitment to good governance, development and poverty reduction – both nationally and internationally Target 8.B: Address the special needs of the least developed countries Includes tariff and quota free access for the LCD's exports; enhanced programme of debt relief for the heavily indebted poor countries and cancellation of official bilateral debt; and more generous ODA for countries committed to poverty reduction Target 8.C: Address the special needs of landlocked developing countries and small island developing States (through the Programme of Action for the Sustainable Development of Small Island Developing States and the outcome of the twenty-second special session of the General Assembly) Target 8.D: Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term	<u>Official Development Assistance</u> 8.1 Net ODA, total and to the LCDs, as percentage of OECD/DAC donors' gross national income 8.2 Proportion of total bilateral, sector-allocable ODA of OECD/DAC donors to basic social services (basic education, primary health care, nutrition, safe water and sanitation) 8.3 Proportion of bilateral ODA of OECD/DAC donors that is untied 8.4 ODA received in landlocked developing countries as a proportion of their gross national incomes 8.5 ODA received in small island developing States as a proportion of their gross national incomes <u>Market Access</u> 8.6 Proportion of total developed country imports (by value and excluding arms) from developing countries and least developed countries, admitted free of duty 8.7 Average tariffs imposed by developed countries on agricultural products and textiles and clothing from developing countries 8.8 Agricultural support estimate for OECD countries as a percentage of their gross domestic product 8.9 Proportion of ODA provided to help build trade capacity <u>Debt sustainability</u> 8.10 Total number of countries that have reached their HIPC decision points and number that have reached their HIPC completion points (cumulative) 8.11 Debt relief committed under HIPC and MDRI Initiatives 8.12 Debt services as a percentage of exports of goods and services
Target 8.E: In cooperation with pharmaceutical companies, provide access to affordable essential drugs in	8.13 Proportion of population with access to affordable essential drugs on a sustainable basis

developing countries	
Target 8.F: In cooperation with the private sector, make available the benefits of technologies, especially information and communications	8.14 Fixed telephone lines per 100 inhabitants 8.15 Mobile cellular subscriptions per 100 inhabitants 8.16 Internet users per 100 inhabitants