DRACUNCULIASIS, ONCHOCERCIASIS, SCHISTOSOMIASIS, AND TRACHOMA

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Abstract

The four diseases discussed in this chapter (dracunculiasis, onchocerciasis, schistosomiasis, and trachoma) are among the officially designated "Neglected Tropical Diseases," and each is also both the result of and a contributor to the poverty of many rural populations. To various degrees, they all have adverse effects on health, agricultural productivity, and education. The Carter Center decided to work on these health problems because of their adverse effect on the lives of poor people and the opportunity to help implement effective interventions. As a result of the global campaign spearheaded by the Carter Center since 1986, the extent of dracunculiasis has been reduced from 20 to five endemic countries and the number of cases reduced by more than 99%. We have helped administer nearly 20% of the 530 million Mectizan (ivermectin) doses for onchocerciasis, which is now being controlled throughout most of Africa, and is progressing toward elimination in the Americas. Since 1999, two Nigerian states have been using village-based health workers originally recruited to work on onchocerciasis to also deliver mass treatment and health education for schistosomiasis and lymphatic filariasis. They now also distribute vitamin A supplements and bed nets to prevent malaria and lymphatic filariasis. Ethiopia aims to eliminate blinding trachoma in the Amhara Region of that highest-endemicity country by 2012, already constructing more than 300,000 latrines and other complementary interventions. Because of the synergy between these diseases and poverty, controlling or eliminating the disease also reduces poverty and increases self-reliance.

Key words: *eradication; disease elimination; disease control; Africa; Asia; Latin America; neglected tropical diseases; dracunculiasis; Guinea worm disease; onchocerciasis; river blindness; schistosomiasis; bilharziasis; lymphatic filariasis; trachoma; malaria; Nigeria; Ethiopia; Sudan; Uganda; Ghana; Cameroon; Brazil; Colombia; Guatemala; Mexico; Venezuela; mass drug administration; Dracunculus medinensis; Onchocerca volvulus; Schistosoma mansoni; Schistosoma hematobium; Onchocerciasis Elimination Program of the Americas; village-based health workers; health education; cloth filters; ABATE Larvicide; Mectizan (ivermectin); Zithromax; albendazole; praziquantel; tetracycline ointment; insecticide-treated bed nets; SAFE strategy; Carter Center; vitamin A deficiency; latrines; trichiasis*

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Introduction

Since its inception 25 years ago, the Carter Center has focused on helping to improve conditions in selected countries that have requested our assistance, initially almost exclusively to promote peace. Work on health and agriculture followed quickly, however, as their relation to promoting peace and reducing poverty became evident and opportunities arose to do more—hence the Carter Center motto of "Waging Peace, Fighting Disease, and Building Hope." The motto of our assistance to health programs, which are under way in parts of Africa and Latin America, is "Fighting Disease and Building Hope at the Grassroots," reflecting our concentration on helping rural villagers to improve their own lives in tangible ways that increase self-reliance and reduce poverty as well as prevent and cure targeted diseases. Our work to help fight the four main diseases discussed in this chapter epitomizes and illustrates the interrelation between the two adverse conditions, poverty and disease, in which poverty is both a contributing cause and a result of these neglected tropical diseases. Singly and in combination, these diseases impair the health, agricultural productivity, and education of affected populations. As summarized below, this work engages village volunteers and ministries of health in more than a dozen African countries and six nations of the Americas, as well as many generous donors, including several corporations.

Dracunculiasis (Guinea worm disease), schistosomiasis (bilharziasis), onchocerciasis (river blindness), and trachoma are all included among the recently designated "Neglected Tropical Diseases" and share those diseases' characteristics of affecting poor neglected populations, mostly in rural areas of Africa, Asia, and/or Latin America. More than 200 million persons on all three continents are believed to suffer from schistosomiasis, about 63 million exhibit clinical signs of active trachoma[1], and more than 37 million have onchocerciasis.[2] Two decades ago, dracunculiasis infected an estimated 3.5 million persons, but fewer than 10,000 still suffer from that disease today, thanks to the successes of the Guinea worm eradication campaign. Many more are still at risk of all four diseases, which also overlap in some populations.

The Carter Center decided to work on these diseases and a few others in keeping with our principles of emphasizing action and results, not duplicating the work of others, accepting the possibility of failure, and the belief that people can improve their own lives with a little outside help. The criteria we used to select these specific diseases were evidence of their adverse effect on impoverished populations, the availability of practical and effective interventions, our view that these diseases were not being addressed adequately (if at all) by others, and our judgment that each disease was susceptible to a data-driven control or eradication approach in partnership with the national authorities and communities concerned.

The global campaign to eradicate dracunculiasis began at the Centers for Disease Control and Prevention in 1980 and has been spearheaded by the Carter Center since 1986. Dracunculiasis (caused by the nematode *Dracunculus medinensis*) is transmitted only to humans who drink contaminated water, typically from stagnant ponds or wells containing tiny copepods (water fleas) that are infected with Guinea worm larvae. The thin adult female worms, up to 1 m (~3 ft) long, emerge through the skin on any part of the body, but usually from the lower limb(s), after a yearlong incubation period during which the victim experiences no signs or symptoms of the

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infection until just before the worm starts to emerge. During the worm's painful emergence, which commonly is associated with secondary bacterial infection of the exit wound, infected persons are incapacitated for periods averaging 2–3 months. Half or more of a village's population may suffer this infection at the same time, and the seasonal period of emergence often coincides with harvest or planting times of peak demand for agricultural labor. This disease thus has a substantial adverse effect on agricultural productivity and school attendance in addition to its primary effect on villagers' health.[3]

People do not become immune after recovering from an infection, and there is no treatment or cure for the disease once a person is infected. But there is no animal or other nonhuman reservoir of this disease, either, and it can be prevented by teaching people to avoid entering sources of drinking water when a worm is emerging, to always filter potentially contaminated drinking water through a fine cloth, by treating contaminated water sources with ABATE® Larvicide (BASF Corp., Mt. Olive, NJ) every 4 weeks, and by providing safe sources of drinking water from borehole wells, for example. E.I. DuPont Corporation and BASF have donated $14 million in nylon filter material and more than $2 million in ABATE Larvicide to the Carter Center for the Dracunculiasis Eradication Program.

By affecting health, agriculture, and education, dracunculiasis is a multifaceted engine of poverty. Economic loses from dracunculiasis are counted in the tens of millions of U.S. dollars, and the economic rate of return on investment in its eradication is estimated at 29%[4] on the sole basis of improved agricultural production. Moreover, many other important benefits have already accrued from the Dracunculiasis Eradication Program, which pioneered the use of village volunteers for reporting cases of disease monthly, for educating other villagers about how to protect themselves, for treating the infection and thus extending rudimentary health services to remote rural communities, and for distributing means of protection—in this instance, nylon filters.[5]

By the end of 2007, 15 of the 20 recently endemic countries had interrupted transmission of dracunculiasis, and two of the remaining five endemic countries are on the verge of eradication in 2008 (Fig. 1). The number of endemic villages has been reduced from 23,735 in 1993 to 2113 in 2007, and the number of cases from an estimated 3.5 million in 1986 to 9889 cases in 2007. Of the individual countries, Nigeria and Uganda have made the most dramatic progress. Nigeria began with more cases (>650,000 in 1989) than any other country but reported only 73 cases in 2007. Uganda had more than 125,000 cases in 1991, stopped transmission in 2003, and has reported zero indigenous cases since. Sudan, which ended a 20+-year-long civil war in 2005, and Ghana, which reported the second-highest number of cases (180,000) in 1989, together account for 99% of all remaining cases. Ghana has struggled to regain its political will since an outbreak of interethnic violence disrupted the Guinea worm program in 1994.[6]

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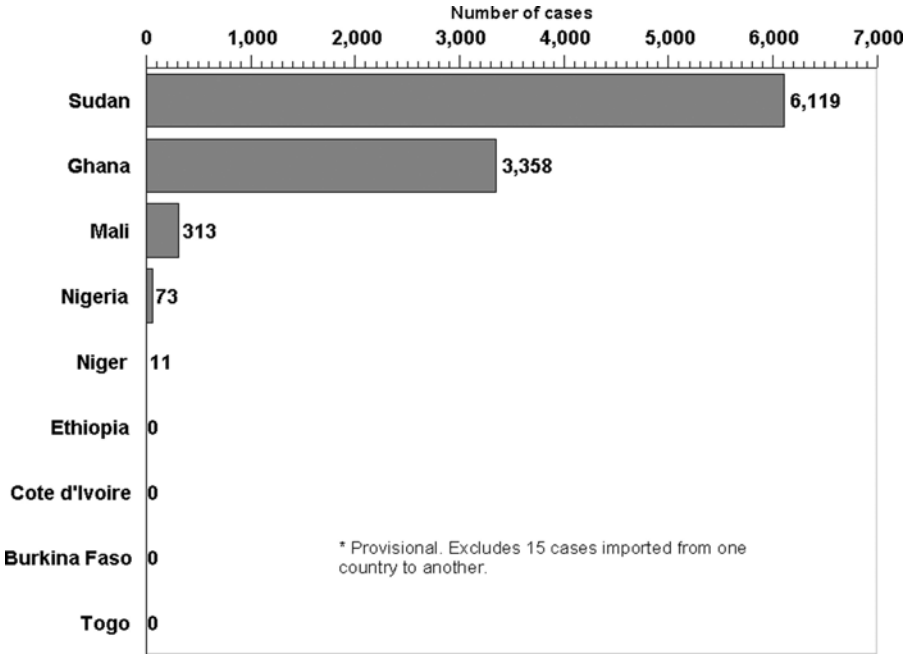

FIGURE 1. Distribution of indigenous cases of dracunculiasis reported during 2007.

Onchocerciasis (caused by *Onchocerca volvulus*) is transmitted to humans by the bite of infected *Simulid* black flies. It is found mostly in Africa, with a few foci in Yemen and six Latin American countries. About 123 million persons are at risk of contracting this infection. These adult filarial worms live for several years bundled together in fibrous nodules, from which they release thousands of microfilariae into the skin and subdermal tissues. Black flies are infected when they feed on infected people. The microfilariae cause the most damage when they accumulate in the eyes. After several years of repeated infections, humans may become blind. Because the black flies breed in fast-flowing rivers, and the disease is most common in association with such locales, it is sometimes called river blindness. The microfilariae in skin produce intense itching, which provokes severe scratching, resulting in disfiguring discoloration and thickening of the skin, which in turn often causes social ostracism. Populations often abandoned fertile farmland near rivers to escape the infection, thus causing significant economic effects.

This disease can be controlled by spraying the breeding sites of the black files with larvicides, and for years that was the main intervention in the highly successful Onchocerciasis Control Program in 11 West African countries. After the New Jersey–based pharmaceutical firm Merck discovered Mectizan® (ivermectin), a drug that effectively suppressed infection by killing the microfilariae when administered orally once a year, that became the (less expensive) intervention of choice to control onchocerciasis. Merck's epochal decision, announced in 1987, to donate Mectizan for as long as needed, in whatever amounts were needed, to help control onchocerciasis, spawned additional programs to control onchocerciasis in the remaining endemic areas of Africa (African Program for Onchocerciasis Control, covering 16 countries) and to eliminate the infection in the six endemic countries of the Americas (Onchocerciasis Elimination Program of the Americas [OEPA]). Merck's donation also provided a less expensive means to consolidate the

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gains of the Onchocerciasis Control Program. The estimated economic rate of return for controlling onchocerciasis is 17%.[7]

By 2007, more than 530 million treatments with Mectizan for onchocerciasis had been approved in 32 countries of Africa, Latin America, and Yemen since 1987. The Carter Center, with the collaboration of Lions Clubs and support of the Lions Clubs International Foundation and other donors, has assisted in providing more than 100 million treatments since 1996, in five African countries (Cameroon, Ethiopia, Nigeria, Sudan, and Uganda) and in all 13 foci in the six affected countries of the Americas (Brazil, Colombia, Ecuador, Guatemala, Mexico, and Venezuela [Fig. 2]). Assessments of the effect of mass drug administration for onchocerciasis in Imo State, one of the nine states being assisted in Nigeria (Fig. 3), have documented reductions in the prevalence of onchocerciasis nodules from 59% to 18% and poor visual acuity from 16.1% to 1% in 7 years.[8] In the Americas, OEPA began in 1993 and administers mass treatments in 13 foci with Mectizan twice per year to help accelerate elimination of the parasite. By 2007, there were no more new cases of blindness from onchocerciasis occurring in the Americas, there were no more eye infections with *Onchocerca volvulus* in nine of the 13 foci, and transmission had been suppressed or stopped in six of the 13 foci.[9] Recent analysis of studies suggests that Mectizan has some macrofilaricidal effect in addition to its microfilaricidal affect. This finding suggests that twice-yearly treatment of all affected communities could eliminate the disease (by also killing adult worms) in 6–7 years rather than the 12–14 years believed just a few years ago. The operational lessons learned by OEPA might be useful in Africa.

FIGURE 2. Carter Center–assisted onchocerciasis control programs.

Human schistosomiasis (caused primarily in Africa by *Schistosoma mansoni* and S. *hematobium*) is believed to be the most common tropical parasitic disease after malaria, and Nigeria has more people (~30 million) affected by schistosomiasis than any other country. Microscopic forms of these parasites penetrate the skin of persons who enter contaminated fresh water, where certain snails release many immature parasites after having been infected themselves by larvae that emerge from eggs deposited in the water by urine or feces of previously infected humans. The adult worms reside mostly in veins of the bladder and/or intestines. The females release tens of

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thousands of spiny eggs that work their way into the intestines or bladder to be excreted with feces or urine. The eggs also damage the bladder, intestines, liver, kidneys, lungs, and other organs, causing bloody urine, bloody diarrhea, heart failure, cirrhosis of the liver, and kidney disease. This debilitating infection can be an occupational hazard for rice farmers and fishermen, but children aged 5–15 years are the ones most heavily infected, because of their exposure to water while playing and swimming. Most public health programs in Africa to control schistosomiasis now involve health education to reduce pollution of water sources by feces and urine of infected humans, as well as annual oral mass treatment of at-risk populations with praziquantel, a highly effective drug that costs US$0.15–$0.20 per treatment. Use of chemicals to kill vector snails may be appropriate in selected circumstances, but this approach is generally too expensive.

The Carter Center is assisting three Nigerian states (Plateau, Nasarawa, and Delta [Fig. 3]) to control urinary schistosomiasis. The center does so by using the grassroots distribution system of health workers and village volunteers established with our assistance earlier for onchocerciasis to also deliver health education and conduct mass drug administration with praziquantel annually in areas affected by both parasites. Since 1999, this program has delivered a cumulative total of 1,079,335 treatments with praziquantel. Studies in a sample of villages in two areas showed a reduction in prevalence of bloody urine (assessed by dipstick) from 47% in 1999 to 8% in 2002, after just 2 years of annual praziquantel treatment.[10] The costs of mapping and the purchase of praziquantel are major constraints to expanding schistosomiasis control efforts nationwide in Nigeria.[11] Because assessing the prevalence of *S. haematobium* by using dipsticks to test the urine samples of school-aged children to determine which communities qualify for mass treatment (according to criteria developed by the World Health Organization) is easier and cheaper than the much more tedious and costly collection and microscopic examination of feces to test for *S. mansoni* infections, programs in these three states focus on urinary schistosomiasis. Carter Center researchers and Nigerian health workers in these programs have shown, however, that about one-half of villages that do not qualify for mass treatment because of urinary schistosomiasis levels would have qualified for treatment if they had also been tested for the intestinal form of the disease.[12] The Carter Center is also engaged in other investigations that are exploring the optimal timing to rotate annual mass treatment after a few consecutive treatment years, from treated communities to other previously untreated communities, to extend the benefits of treatment to as many people as possible by using limited funds available to purchase the drug.

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FIGURE 3. Carter Center–assisted states in Nigeria.

Lymphatic filariasis (LF) in Africa is caused by *Wuchereria bancrofti*, a filarial worm related to the parasite that causes onchocerciasis, but LF is transmitted (in Africa) in rural areas by the same mosquito (*Anopheles*) that transmits malaria. The adult worms cause swelling of limbs (lymphedema and "elephantiasis") and genital organs, as well as painful recurrent attacks of acute adenolymphangitis and fever. In Africa, LF microfilariae can be almost completely suppressed by annual single-dose combination therapy with Mectizan (also donated by Merck for LF in Africa) and albendazole (donated by GlaxoSmithKline). In two states of Nigeria (Plateau and Nasarawa), the Carter Center–assisted onchocerciasis control program has also provided a platform10 from which to mount integrated disease control efforts against LF in addition to schistosomiasis, as well as against malaria (by distributing bed nets that prevent malaria and LF) and vitamin A deficiency (by providing vitamin A supplementation to young children). Since 1999, in the two-state area we have helped administer cumulative totals of 7,709,058 Mectizan treatments for onchocerciasis; 17,657,335 Mectizan and albendazole combination treatments for LF; 1,010,808 praziquantel treatments for urinary schistosomiasis, and 383,285 vitamin A supplementation treatments to young children. In Nigeria, we are also helping to investigate the feasibility of eliminating LF transmission by use of mass drug administration and insecticide-treated bed nets.[13] The same village-based health workers providing mass treatment have also distributed 176,369 insecticide-impregnated nets for LF and malaria prevention since 2004.

Trachoma is the leading preventable cause of blindness worldwide, with some 10% of the world's population at risk of blinding trachoma. This chronic bacterial infection of the conjunctiva and cornea is transmitted from one infected person to another by contaminated hands, cloths, and flies. Scarring of the conjunctiva lining the inside of the upper eyelid from repeated infections in childhood causes the lid to turn in upon itself, bringing the eyelashes into contact with the eye (trichiasis), which leads to painful abrasion of the sensitive cornea, which can rapidly lead to blindness. Trachoma is associated with poverty, and by causing dependency and disability the

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condition contributes to keeping impoverished communities poor.[14] In most hyperendemic areas, 75% of those blinded by trachoma are women. The specific flies that transmit this infection, *Musca sorbens*, breed almost exclusively in human feces that are deposited on the ground.[15] The World Health Organization has endorsed an evidence-based integrated control program for trachoma known as the SAFE strategy (an acronym derived from [1] surgical correction of trachomatous trichiasis, [2] antibiotic treatment of infected and at-risk people, [3] face washing, and [4] environmental sanitation) to suppress active infections, reduce person-to-person transmission, and reduce breeding of the flies in question.[16] The pharmaceutical company Pfizer, Inc. (NY, NY), is donating large quantities of its antibiotic Zithromax® (azithromycin) to treat persons at risk as part of the SAFE strategy.

The Carter Center is helping six African countries eliminate blinding trachoma in parts of their national territories. Major funding for this assistance is provided by the Conrad N. Hilton Foundation (Ghana, Mali, Niger, and Nigeria) and the Lions Clubs International Foundation (Ethiopia and Sudan). Our largest trachoma project is in the Amhara Region of Ethiopia, in association with the regional and national Ethiopian health authorities and local Lions Club members. Ethiopia is believed to be the most highly endemic country in the world for trachoma, and approximately 40% of the active trachoma in Ethiopia is in the Amhara Region. The common goal of a partnership of Ethiopian health authorities, local Lions Club members, and the Carter Center is to eliminate blinding trachoma in the Amhara Region by 2012. Since this bold initiative got under way in 2002, it has helped implement trichiasis surgeries for a cumulative total of 93,155 persons (14% of the estimated backlog of 643,000 persons needing such surgery), administered a total of 10,121,418 Zithromax and 1,031,064 tetracycline treatments, conducted health education about trachoma in 640 of the 3231 schools in the region, and stimulated the construction of 354,179 household latrines and 119 water points. Because traditional customs forbade adult females from relieving themselves in public, women quickly mobilized to support latrine building for the sake of their own privacy and convenience, with impressive results. After several months of using a latrine, one woman declared, "We will never go back [to defecating on the ground, mostly at night]."Figure 4 shows the cumulative latrine construction in the region and the annual targets for latrine construction over the next 5 years to reach Millennium Development Goal 7, target 10 (halve by 2015 the proportion of people who do not have access to improved sanitation). As with mass drug administration for the other diseases, the explosion in construction and use of latrines will yield health benefits beyond limiting the breeding of eye-seeking flies that transmit trachoma.

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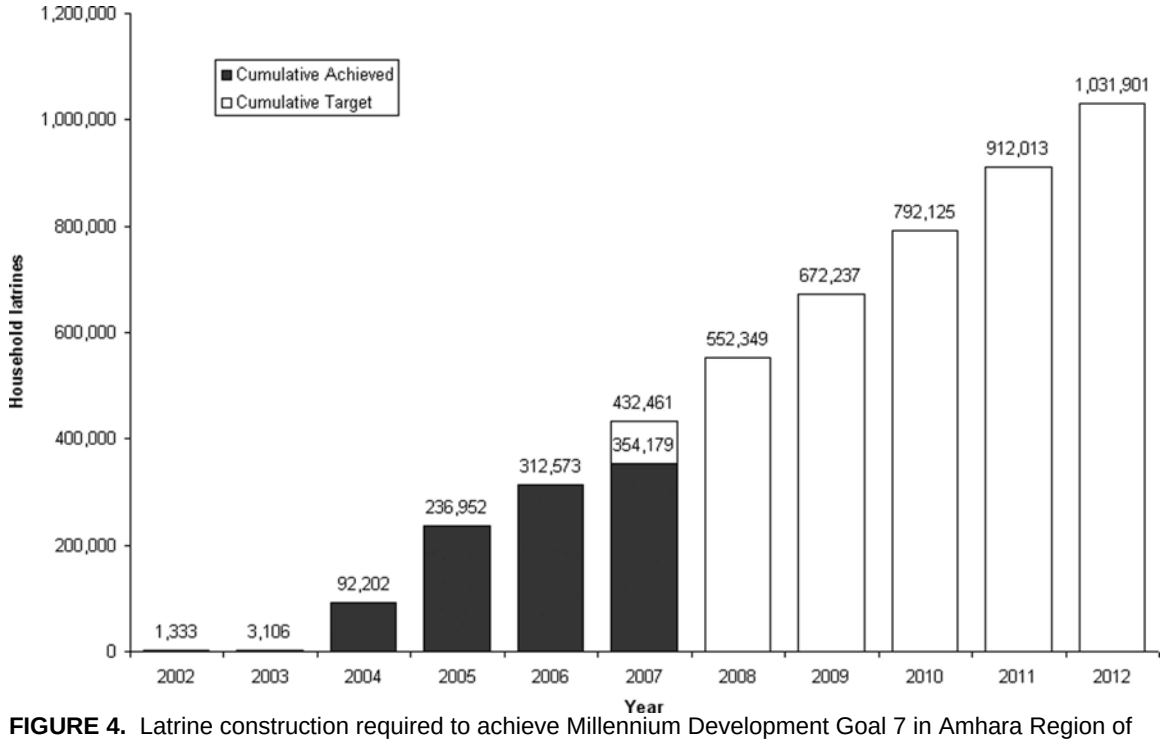

FIGURE 4. Latrine construction required to achieve Millennium Development Goal 7 in Amhara Region of Ethiopia by 2012.

In 2007, at the request of the ministry of health of Ethiopia, the Carter Center purchased and assisted the distribution of 3 million long-lasting insecticidal bed nets (LLINs) to help prevent malaria in the areas we are assisting to combat trachoma and onchocerciasis (Fig. 5), using the same health workers and infrastructure. This action was part of Ethiopia's successful campaign to distribute 20 million LLINs to protect its entire at-risk population of 50 million persons before the end of 2007.

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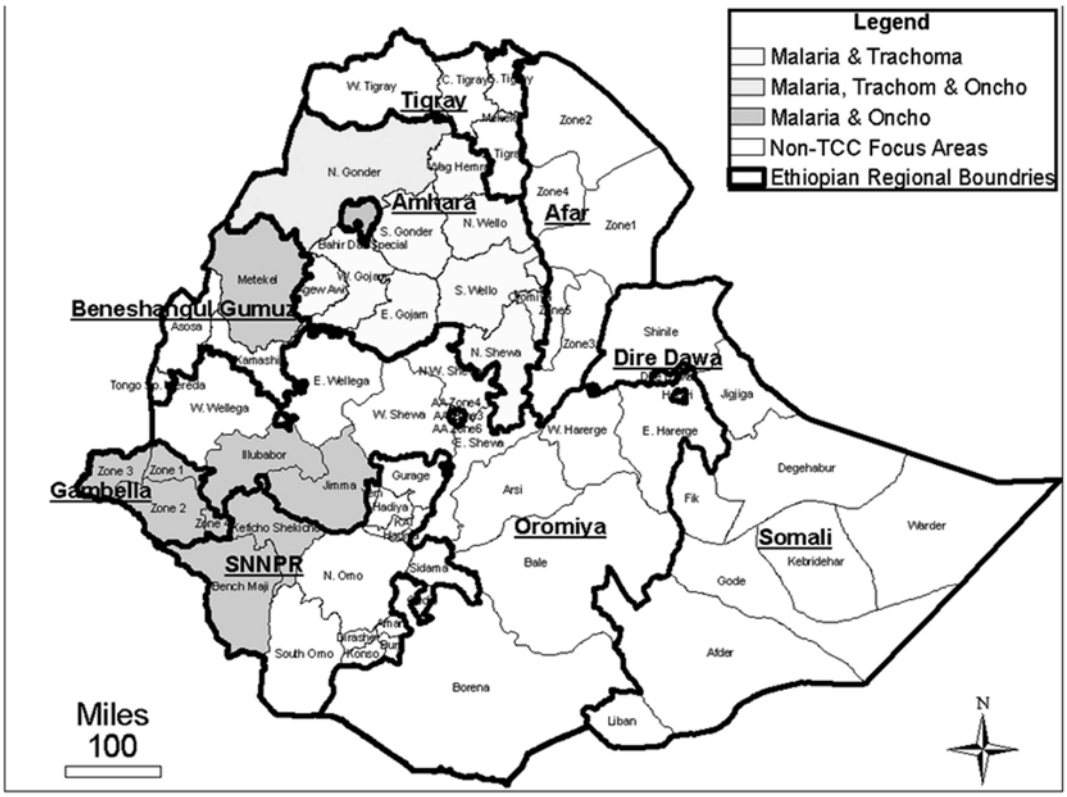

FIGURE 5. Carter Center (TCC)–assisted control programs in Ethiopia.

Conclusion

In addition to the many direct benefits of these programs in improved health and nutrition, there are many indirect benefits. The antihelminthic drugs used have ancillary benefits because they are also effective against other parasitic intestinal infections, such as *Ascaris* and hookworm. A reduced parasitic burden also improves the cognitive ability of children and results in fewer malarious episodes,[17 18 19 20] reduced anemia in pregnant women, higher birth weight in newborns, and reduced infant and child mortality.[21] The antibiotic for trachoma is also effective against respiratory infections, especially in children, and has some antimalaria effect. The use of LLINs to prevent malaria also prevents some other vectors from transmitting diseases, and use of latrines built to reduce transmission of trachoma also prevents transmission of other diseases such as diarrhea, intestinal parasites, and schistosomiasis.

The campaign against dracunculiasis is unique among the interventions described in this report, because it is the only eradication program among them. However, the OEPA program in Latin America is working to eliminate onchocerciasis with some relevance to Africa, the LF effort in Nigeria is testing the feasibility of eliminating LF transmission in Africa, and the trachoma program in Ethiopia is working to eliminate blindness due to trachoma in a sustainable way with ramifications for a worldwide effort. All four programs illustrate the potential direct and indirect benefits of village-based interventions that engage the power of local mobilization at the community level. To do so successfully requires respect for local knowledge, social structures,

and dignity, as well as assiduous attention to details in the selection, training, retraining, supervision, encouragement, feedback, and provision of supplies to the village volunteers.

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Conflicts of Interest

The authors declare no conflicts of interest.

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