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B.A.
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2010

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Abstract

Assessing Performance of Community-Directed Treatment with Ivermectin between Onchocerciasis Control and Elimination Programs in Uganda

By: Deanna K. Tollefson

Purpose: Despite the success of community-directed treatment with ivermectin (CDTI) to control onchocerciasis, onchocerciasis continues to annually cost the world one million DALYs. Despite effective CDTI in Uganda, 2.5 million people remain at risk for onchocerciasis. To address this, in 2007 Uganda changed its onchocerciasis programs from control to elimination, replacing once-annual with twice-annual distribution of ivermectin. This evaluation assesses the effectiveness of Uganda's elimination program in comparison to its control program, and it determines factors associated with CDTI success to ensure Uganda can move successfully toward elimination.

Methods: Annual surveys collected data on CDTI from households in Uganda. Data were compared under onchocerciasis control and elimination programs (2004-2006 versus 2007, 2009, and 2010, respectively). Ivermectin treatment coverage was analyzed at the household, community, and district level, with at least 90% ivermectin coverage of the eligible population defined as success. Multivariate logistic regressions were used to identify associations between CDTI programming variables and receipt of ivermectin. Trends in CDTI programming were compared over time.

Results: Approximately eleven thousand persons were sampled from 2004-2010, with ≥90% reporting to have received ivermectin each year. Ivermectin coverage increased under the elimination program, with 97.1% and 94.0% of respondents receiving at least once-annual and twice-annual treatment, respectively, compared to 92.3% receiving ivermectin under the onchocerciasis control program. Compared to the control program, the percentage of communities achieving 90% ivermectin coverage was greater for once-annual treatment but lesser for twice-annual treatment under elimination policy. Personal investment in CDTI was strongly associated with receiving once-annual treatment in both control and elimination programs, whereas the location of treatment and coordination with the kinship unit were strongly associated with twice-annual receipt of ivermectin. The elimination program increased convenience of ivermectin treatment, but it may be less rooted in the community than the control program.

Discussion: To date, Uganda's onchocerciasis elimination approach has been more effective in providing ivermectin than the control program, but increased efforts are necessary to ensure twice-annual ivermectin coverage is achieved in all communities. Factors extrinsic to the community involvement in CDTI must be investigated to better understand variables that influence twice-annual receipt of ivermectin.

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Introduction

Onchocerciasis is a parasitic disease endemic to 37 countries in sub-Saharan Africa, six countries in Latin America, and Yemen, placing more than 120 million people at risk for acquiring infection (Brattig 2009; Gustavsen et al 2011). Onchocerciasis is caused by infection of filarial larvae of *Onchocerca volvulus*, a nematode, which is transmitted through bites of certain *Simulium* black flies, specifically *Simulium damnosum* complex in Africa (CDC 2010; Katabarwa et al 2008; Mackenzie et al 2012). After an infected female black fly takes a blood meal, *O. volvulus* larvae enter the person's skin where they develop into adult filariae, which can live for more than fifteen years in subcutaneous nodules throughout the body (CDC 2010). As they reproduce, the microfilariae exit the nodules, inducing an immunological response that can frequently cause adverse reactions in the host (Katabarwa et al 2008; Mackenzie et al 2012). As the microfilariae enter the blood, they are also able to infect *Simulium* black flies that feed on the infected person, which continue the spread of onchocerciasis (CDC 2010; Katabarwa et al 2008; Mackenzie et al 2012).

It is currently estimated that 26-37 million persons are infected with *Onchocerca volvulus*, with 99% of infections occurring in rural Africa (Brattig 2009; Gustavsen et al 2011; Hotez 2011; Mackenzie et al 2012; WHO 2009). Recently, rapid epidemiological mapping has suggested that more than 102 million additional people in nineteen African countries are at high risk for becoming infected by *O. volvulus* (WHO 2011). As the black fly vector breeds in fast-moving rivers, rural communities living in fertile valleys around rivers or those living within forests near river banks are most at-risk for infection (Katabarwa et al 2008; WHO 2011).

Ivermectin is a highly effective drug to use against onchocerciasis, but it kills only the *Onchocercerca volvulus* larvae, and not the adults that easily live more than fifteen years within the host. As such, treatment must occur annually at least over a minimum of fifteen years to ensure the adult nematodes have died so larvae can no longer be produced in the body (Babalola 2011; Hotez 2011; WHO 2009).

Community-directed treatment with ivermectin (CDTI) is the primary method used to treat and control onchocerciasis. CDTI is a community-based mass drug administration approach that relies upon citizens to provide ivermectin for everyone in their communities (Diawara et al 2009; Katabarwa et al 2008; WHO 2009). Despite the widespread success of CDTI programs, the latest estimates suggest that onchocerciasis continues to cost the world one million DALYs annually (Boatin and Richards 2006; Brattig 2009).

Onchocerciasis in Uganda

In Uganda, onchocerciasis is endemic in 35 districts, placing up to 2.5 million persons at risk for contracting and developing the disease (GoU MoH 2010). In the past decades, onchocerciasis has primarily been endemic in western and northern portions of Uganda and in the Democratic Republic of Congo and Sudan, which border the country to the west and north, respectively. Historically, onchocerciasis existed in Uganda's central region near Lake Victoria, but the disease was eliminated from here prior to the 1980s. In eastern Uganda, there remains a small pocket covering the Mt. Elgon area where onchocerciasis is still endemic (GoU MoH 2007) (See Figure 1).

From 1991 - 2006, the country adopted a strategy to control onchocerciasis, relying primarily upon annual CDTI, that provided people one-dose of ivermectin per year, and to a lesser extent, vector spraying[1]. During this time, more than 70% of the country's total population reported to have received one dose of ivermectin per year, demonstrating the nation's success at controlling onchocerciasis. However, even with this successful ivermectin coverage, onchocerciasis remained a problem that needed to be addressed for a seemingly indefinite time period, as the program aimed to control and not eliminate the disease. As such, policy makers grew increasingly fatigued with the continuous distribution of ivermectin. Based on Uganda's demonstrated success and growing fatigue with indefinite CDTI, in 2007 the country adopted a more ambitious goal: nationwide elimination of onchocerciasis. This new goal was largely inspired to revive enthusiasm to battle onchocerciasis so

[1] Vector spraying occurred primarily in Itwara and Mpamba-Nkusi, two foci of western Uganda.

that the disease could be permanently resolved and ivermectin distribution someday halted (GoU MoH 2010). To achieve this goal, Uganda decided to shift from annual to semi-annual CDTI, in which twice yearly distribution of ivermectin would be provided.

The elimination strategy that used semi-annual CDTI was introduced in 2007 on a rolling basis in 13 districts primarily in the country's eastern, western, and southwestern districts (GoU 2007, GoU MoH 2010). Additional districts were added in subsequent years, being implemented lastly in Uganda's northwestern districts closest to the DRC and northern districts bordering South Sudan, which traditionally retained the highest transmission of onchocerciasis (GoU MoH 2010).

To achieve onchocerciasis elimination, the Government of Uganda continues to partner closely with non-governmental organizations, particularly the Carter Center. The Carter Center has been integral in supporting the development, implementation, and monitoring of Uganda's national onchocerciasis control and elimination programs and has been integral in assisting the nation shift from annual to semi-annual CDTI (GoU MoH 2010).

Literature Review

Significance of Onchocerciasis

Widespread infection of onchocerciasis is problematic because onchocerciasis causes substantial morbidity, affecting the physical, mental, social, and economic wellbeing of individuals and their communities. Onchocerciasis remains the leading cause of blindness in Africa (Katabarwa et al 2008) and the second leading cause of preventable blindness in the world[2] (WHO 2011). Even more common than ocular disorders, onchocerciasis causes severe dermatological problems, including debilitating itching, depigmentation, and disfiguring lesions (Mackenzie et al 2012; WHO 2011), which can also cause the development of secondary skin infections (Okeibunor et al 2011).

[2] Blindness is such a well-known outcome for the disease that onchocerciasis is commonly called "River Blindness"; the black fly vectors breed in fast-moving rivers and infected individuals commonly experience ophthalmological complications when microfilariae enter the eye (Katabarwa, et al 2008). The iconic image of onchocerciasis has also long been a child leading a blind man through a rural village (Mackenzie, et al 2012).

Ultimately, people with high *Onchocercerca volvulus* loads have been found to have shorter lifespans, even in the absence of other symptoms (Brattig 2009).

The dermatological and ocular ailments also cause social and economic problems for infected individuals (Amazigo et al 2007). Skin disfiguration is a source of stigma that has been found to cause psychosocial distress, due to the negative perceptions from non-diseased community members (Brieger et al 1998; Murdoch et al 2002) and personal fears related to physical disfiguration, such as finding a marriage partner (Murdoch et al 2002; Vlassoff et al 2000). Individuals with onchocerciasis have also been found to suffer psychosocial distress because blindness or intense itching can decrease their ability to work, thereby diminishing their economic wellbeing (Amazigo et al 2007; Brenton 1998; Okeibunor et al 2011; Oldaepo et al 1997; Vlassoff et al 2000). For example, farmers with onchocerciasis have been found to till less land and be involved with fewer external economic ventures than those without the disease (Oldaepo et al 1997). Likewise, in households headed by a person with onchocerciasis, children are two-times more likely to drop out of school than those living in households headed by a guardian that did not have this disease (Brenton 1998).

Response to Onchocerciasis

As a result of the severe and widespread effects of onchocerciasis, for years alliances of governmental and non-governmental agencies have been organized to combat the disease. The World Health Organization's Onchocerciasis Control Program (OCP) was the first organization that mobilized to decrease the consequences of onchocerciasis. It ran from 1974-2002 in eleven West African countries, focusing predominantly on vector elimination (Babaloa 2011; Brattig 2009; Molyneux 2005). Larvicides were applied weekly to black fly breeding sites, achieving interruption of parasite transmission in these areas (Brattig 2009; Molyneux 2005). However, in 1987, the pharmaceutical company, Merck, promised to indefinitely donate ivermectin (Mectizan®) to persons residing in locations where onchocerciasis was endemic (Cupp et al 2010; Gustavsen et al 2011; WHO 2009). As this drug resolves an individual's onchocerciasis infection, mass drug administration

(MDA) of ivermectin supplemented and eventually replaced vector elimination as the primary means to control onchocerciasis (Brattig 2009; Molyneux 2005).

The African Programme for Onchocerciasis Control (APOC), which began in 1995 and will run until 2015, expanded upon the efforts, knowledge and experience of the OCP to eliminate onchocerciasis as a public health problem from the rest of Africa (Molyneux 2005; WHO 2011; WHO 2012). Like the OCP, APOC is coordinated under the WHO, but it is larger than the preexisting organization. It is active in nineteen countries[3] and relies on substantial involvement from ministries of health and both local and international non-governmental organizations (Bush 2011; WHO 2012). APOC utilizes CDTI as its primary strategy to address onchocerciasis (Molyneux 2005; WHO 2011; WHO 2012), although vector control continues to be a cost-effective method for control in small, isolated communities where the vector can easily be eliminated in a short period of time (Brattig 2009). An onchocerciasis program also exists in the Americas. Led by the Carter Center, the Onchocerciasis Elimination Program for the Americas (OEPA) began in 1991 and has addressed onchocerciasis through CDTI in Brazil, Ecuador, Venezuela, Columbia, Guatemala, and Mexico (Gustavsen et al 2011; Molyneux 2005).

APOC and OEPA provide financial support to CDTI projects for five years, with the goal to build capacity so that ivermectin distribution is sustainable over time (Katabarwa et al 2008). In CDTI, Ministries of Health in conjunction with local NGOs provide ivermectin and strengthen the capacity of communities to successfully distribute ivermectin and engage households in the fight against onchocerciasis (Diawara et al 2009; WHO 2009). Select community members are chosen to be community-directed distributors (CDDs) by community health workers (CHWs) and then trained to actively provide treatment for and education on onchocerciasis to the entire community (Katabarwa et al 2008). In 2010, over 500,000 CDDs and 50,000 CHWs were trained or retrained in

[3] APOC countries include: Angola, Burundi, Cameroon, Central African Republic, Chad, Congo, Democratic Republic of Congo, Ethiopia, Equatorial Guinea, Gabon, Kenya, Liberia, Malawi, Mozambique, Nigeria, Rwanda, Sudan, Tanzania and Uganda (WHO 2012)

sixteen countries in Africa to organize successful CDTI campaigns. In total, they treated an estimated 75.8 million people for onchocerciasis (WHO 2011).

APOC countries have largely implemented annual CDTI, whereas OEPA countries have used semi-annual (2x/year) or multi-annual (up to 8x/year) CDTI (Cupp et al 2009; Duerr et al 2011; Molyneux 2005). Both programs have been so successful at reducing infection of and morbidity due to *O. volvulus* that onchocerciasis control measures have been described as some of the most important in global health programming in the past thirty years (Molyneux 2005). To date, more than 900 million doses of ivermectin have been given in 34 countries through these onchocerciasis control programs (Mackenzie et al 2011). The majority of community members, both children and adult, have recognized CDTI to improve their wellbeing physically, socially, mentally, and economically (Amuyunzu-Nyamongo et al 2011; Okeibunor et al 2011). Most recently the success and frequency of CDTI has encouraged additional programs to be added to CDTI (i.e, Vitamin A and bed nets) (CDI Study Group 2010; Molyneux 2005; Katabarwa et al 2010-a).

Factors Affecting CDTI Success

The Carter Center defines its onchocerciasis programs as successful if they achieve at least 90% ivermectin coverage of the eligible population[4] (Katabarwa et al 2010-a). Research and evaluations have been conducted to illuminate factors that affect the success of CDTI, particularly in Uganda, so that ivermectin distribution may be maximally effective (Katabarwa, et al 2010-a, 2010-b, 2008, 2005, 2001-a, 2001-b; Katabarwa, Habomugisha, and Richards 2002, 2000, 1999; Katabarwa 2002). Primary factors that studies have analyzed include (1) degree of community involvement in the CDTI process, including active decision-making regarding the execution of CDTI, attendance at health-education sessions by household heads, community involvement in selecting the community-based distributors, community involvement in choosing the distribution method for CDTI, and community member involvement in choosing how to reward community-based distributors (Katabarwa, Habomugisha, and Richards 2000); (2) location where ivermectin was distributed

[4] All persons living in areas that place them at-risk for onchocerciasis.

(Katabarwa, Habomugisha, and Richards 2000); (3) degree of female involvement in the CDTI process (Katabarwa 2002; Katabarwa et al 2001-b); (4) the use of kinship in CDTI (Katabarwa et al 2010-b); and (5) the number or additional responsibilities and activities, other than ivermectin distribution, given to community drug distributors (Katabarwa et al 2010-a, 2005).

The literature strongly suggests that preserving the community-based nature of CDTI is essential to its continued success. A past evaluation of CDTI in Uganda has demonstrated that community involvement, specifically inclusion in the selection of persons distributing ivermectin, choosing how the ivermectin is distributed, and participation in health-education sessions is highly associated with household participation in ivermectin campaigns (Katabarwa, et al 2000). Similarly, CHW and CDD in Uganda were found to be more successful if they were selected by their peers (Katabarwa 2010-b). Conversely, they were more likely to leave their role as CDD/CHW if they were not chosen by their peers (Katabarwa et al 2005). Increased involvement in implementing and participating in CDTI has also been suggested to increase community pride and cohesion (Katabarwa, et al 2000).

Although evaluations have shown mixed results for how the location of ivermectin distribution is associated with receiving treatment, it is clear that proximity to one's house or compound is related to higher levels of treatment. More importantly, it has been found that implementing treatment at the kinship level dramatically increases success by decreasing the distance people must travel to receive treatment, increasing the involvement of the kinship unit, and subsequently increasing trust in CDTI (Katabarwa et al 2002-b, Katabarwa et al 2001). Moreover, as women's movements are traditionally restricted outside of the kinship zone, implementing treatment at the kinship level has been found to increase female involvement in CDTI, and in turn, increase overall ivermectin coverage (Katabarwa et al 2002-b, Katabarwa et al 2001). Employing a CDD to work with their specific kinship unit has been found to particularly increase a household's willingness to accept ivermectin treatment (Katabarwa et al 2001). As the notion of kinship becomes better understood, it appears that working within the kinship zone is increasingly essential to retain support and achieve success in all aspects of CDTI (Katabarwa 2010-b).

The associations between a variety of other CDTI components with ivermectin treatment levels have also been investigated. Integrating health activities and health education with CDTI has been found to be especially associated with increased receipt of ivermectin at the household level (Katabarwa et al 1999; Katabarwa et al 2005). The relationship between provision of gifts to CDD/CHW and receipt of ivermectin is more muddled. One study showed cash incentives decreased success of CDDs, while provision of personal gifts to CDDs, a normal custom in sampled communities, had no relationship on treatment (Katabarwa, et al 1999). The knowledge and abilities of CDDs has also been found to be essential for success of CDTI. A past evaluation in Uganda has provided evidence on the importance of training and retraining health workers and community workers involved in CDTI to improve the program's sustained effectiveness (Katabarwa, et al 2002). To date, the effectiveness of ivermectin distribution when partnered with other programs, such as malaria nets or vitamin A distribution, is controversial (CDI Study Group 2010; Katabarwa et al 2010-a). There is also little research on how the frequency of ivermectin distribution per year affects sustained success of CDTI. Factors such as weather events and political stability are known to be just a few of the many exterior variables affecting success of CDTI (Katabarwa et al 1999).

Shifting from Control to Elimination

Onchocerciasis is coming increasingly close to being eliminated in Latin America (Mackenzie et al 2012). OEPA has demonstrated unprecedented success at interrupting onchocerciasis transmission through implementing mass ivermectin treatments providing a minimum of twice annual ivermectin treatment to at least 85% of the population in endemic areas (Cupp et al 2009; Mackenzie et al 2012). Although many factors contributed to successful elimination in Latin America, ensuring at last 85% of the population received multiple treatments annually was viewed as the primary reason for such rapid success (Cupp et al 2010).

OEPA's recent success has made some countries in Africa reanalyze the feasibility of onchocerciasis elimination in Africa. As APOC has traditionally been a control program, it has relied on annual distribution of ivermectin. However, Latin America's success due to increased frequency of ivermectin distribution has propelled APOC to initiate a dialogue on the feasibility of onchocerciasis elimination in Africa if frequency of treatment is increased from once to twice or more yearly (Duerr, et al 2011, WHO 2009). Recent studies in endemic communities in Africa support this thought, suggesting that onchocerciasis elimination can be a reality in Africa if high ivermectin coverage remains continuous (Cupp et al 2010; Mackenzie et al 2012). As a result, there is an increasing push to redefine APOC as an elimination program (Mackenzie et al 2012). Based on current medicine and technologies, semi-annual CDTI is the most attractive strategy to achieve elimination, especially in non-hyperendemic areas (Basanez 2006). As such, some African countries, specifically Uganda, have transitioned from promoting annual to semi-annual CDTI **(**Diawara et al 2009; Duerr et al 2011).

However, the evidence is not conclusive that this elimination strategy will work in Africa as it did in Latin America, and despite early successes of semi-annual CDTI, it remains debatable whether semi-annual treatment will enable onchocerciasis to be eliminated from Africa (Duerr et al. 2011; Katabarwa et al 2008; NA – CMAJ 2009). Administering semi-annual CDTI effectively requires increased human capacity, which may not be feasible in the African context, especially as funds and motivation for ivermectin distribution wane (GoU MoH 2010; Mackenzie et al 2012). For example, high attrition of CDDs, perpetual demands for monetary incentives (Katabarwa et al 2010-b), and waning dedication of policy makers (GoU MoH 2010) have challenged the success of once-yearly CDTI in Uganda. It is believed by some school of thought that increasing the number of CDTI annually could increase the demands of the CDD and could subsequently decrease their ability to participate as fully in CDTI. Likewise, shortage of CHWs, high mobility of populations, and the extreme remoteness of the most at-risk villages suggest that the capacity to successfully deliver CDTI at least twice-annually to endemic areas in Africa may not exist (Brattig 2009; NA – CMAJ 2009).

Even if such external factors were remedied, many scientists believe that onchocerciasis elimination is impossible to achieve in all endemic areas through use of only ivermectin programs and that indefinite treatment is inevitable for continued control of the disease (Katabarwa 2008; WHO 2009).

Regardless of control or elimination, onchocerciasis programs are facing increased challenges because annual ivermectin distribution is unlikely to be maintained indefinitely. Such programs pose high risk for public and donor fatigue, especially when resources are tight (Katabarwa et al 2010-a; Mackenzie et al 2012; Molyneux 2005). Moreover, indefinite distribution of ivermectin encourages resistance, which is becoming of increasing concern as it being noted with increased frequency (Babaloa et al 2011; Katabarwa 2008; Mackenzie et al 2012; Molyneux 2005).

Purpose of Study

As Africa shifts from annual to semi-annual CDTI to encourage onchocerciasis elimination, it is essential that current program performance be maintained. Program coordinators must ensure that communities continue to deliver ivermectin treatment annually to ≥90% of the eligible population. Strong monitoring of ivermectin coverage, program efficacy, and drug resistance is therefore critical to understand and ensure treatment coverage under the elimination strategy is as successful as it was under the control program (Smits 2009). Specifically because of Uganda 's leading role in onchocerciasis control and elimination, it is crucial that program coordinators understand the similarities and differences of program factors associated with effectiveness in annual and semi-annual CDTI. Although there have been multiple studies evaluating annual CDTI in APOC countries (Katabarwa, et al 2010-a, 2010-b; Katabarwa, Habomugisha, and Richards 2002, 2000, 1999; Katabarwa 2002), semi-annual treatment is novel in APOC countries and evaluations on it have not yet been conducted (Smits 2009). Moreover, as the Government of Uganda is leading the APOC shift from annual to semi-annual distribution, it is of utmost importance that the program understands how factors associated with programmatic success differ between control and elimination CDTI programs.

As such, the purpose of this study is to assess the success of Uganda's onchocerciasis elimination program in delivering two rounds of ivermectin annually in comparison to the previous onchocerciasis control program which delivered one round of ivermectin per year. The study was also conducted to elucidate factors that are associated with a household's choice to receive ivermectin treatment and understand how these factors differ between elimination and control programs. This evaluation will particularly assess the following objectives:

1. ***Objective One:*** Compare the level of ivermectin coverage achieved through control and elimination CDTI programs.
2. ***Objective Two:*** Determine what programming variables, if any, are associated with households succeeding or failing to receive ivermectin treatment in onchocerciasis elimination programs and assess how these associations compare with control programs.
3. ***Objective Three:*** Examine trends in CDTI programming between control and elimination programs in light of variables found to be associated with CDTI success and failure.

In accomplishing these aims, this study will increase Uganda's understanding of its current elimination program and the challenges that must be addressed to maximize success and achieve elimination. The results will also enable the Carter Center to provide increased evidence-based programming assistance to Uganda to help it maximize performance. The lessons learned may be extended to neighboring APOC countries that are considering the shift from onchocerciasis control to elimination programs.

Methods

This analysis uses data from the 2004-2010 annual household CDTI program monitoring surveys that the Carter Center implemented through multi-stage random sampling in Ugandan districts where onchocerciasis control/elimination programs were present. Almost eleven thousand households were sampled from 2004-2010, with 4,996 and 5,847 households being interviewed during the onchocerciasis control (2004-2006) and elimination (2007-2010) periods, respectively.

Seven districts were sampled from 2004-2006, while eight were sampled from 2007-2010. Approximately thirty households were surveyed per community from 2006-2010, while ten households were surveyed in each sampled community in 2004 and 2005 (Table 1). Surveys were not conducted in 2008 because expansion of twice-yearly treatment activities and national redistricting, which required extra health workers to be trained, consumed communities' resources and energy.

Study Areas: During the onchocerciasis control program, the following districts were sampled in the given years: Kanungu, Kisoro, Mbale, Moyo, and Nebbi in 2004; Kanungu, Kasesse, Kisoro, Mbale, and Moyo in 2005; and Kisoro, Manafwa, Moyo, and Nebbi in 2006. Under Uganda's onchocerciasis elimination policy, the following districts were sampled: Kamwengye, Kanungu, and Mbale in 2007; Bududa, Hoima[5], and Kanungu in 2009; and Buhweju, Kabale, and Rubirizi in 2010. Kanungu and Mbale district were the only districts sampled in both control and elimination periods. Otherwise, as a result of random sampling, the surveyed districts differed between control and elimination years (Figure 2).

Sampling Design: For each year of this study, multi-stage random sampling was used to select districts, sub counties and communities where surveys were implemented at the household level (Table 1). In each selected community, a list of households was generated using community registers. The first household to interview was selected by using a random number table. Subsequently, every fifth household was selected until the required number of households in the community was met. Selection was conducted at a 95% confidence level for homogenous populations (Salant and Dilman 1994). At least three districts were randomly selected each year. Available funding dictated the number of sub-districts (health areas) and communities that were chosen, but enough districts, sub-districts, and communities were sampled to ensure that there was a maximum 5% sampling error.

[5] NB: At the launching of the onchocerciasis elimination policy in 2007, Hoima had not embraced the kinship approach as part of its CDTI program.

Survey Implementation: In each of the selected households, the household head, normally the adult male or female present during the time period of CDTI activities, was given the survey through a face-to-face interview. Trained members of the community, including teachers, retired civil servants and high school graduates, conducted the interviews. To minimize bias, no interviewers interviewed persons in their own communities.

Survey Instrument: The survey used in this evaluation was approximately twenty questions in length. The survey was validated and versions of it were used over multiple years in Uganda and other African countries in which the Carter Center assists ministries of health to control or elimination onchocerciasis. The survey from each year contained identical questions, although surveys conducted in 2009 and 2010 also contained questions about malaria that were excluded in this analysis.

The primary objective of the survey was to assess ivermectin coverage. To do this, individuals were asked if they had received ivermectin in the past year. For surveys assessing the elimination program, individuals were also asked if they had received ivermectin two-times in the past year. In addition, the surveys gathered household-level data on CDTI programming, including personal involvement in CDTI and the logistics of CDTI within the community. Variables related to personal involvement that were assessed included: personal involvement in deciding treatment location, personal mobilization of CDTI, personal participation in selection of CDTI distributors (CDD/CHW), personal attendance at health education sessions, and providing CDD/CHW with tokens of gratitude. Variables related to CDTI logistics that were assessed included: the location of treatment, the distance of treatment from the person's household, the method by which CDD/CHW were selected, and the method by which the treatment location was decided. In addition, the survey asked questions related to the household's overall satisfaction with the CDTI services and the intent to return for treatment in the following year.

Data Analysis: Ivermectin treatment coverage was compared between the years of the onchocerciasis control and onchocerciasis elimination programs. The percent coverage of ivermectin treatment was calculated for each community and district per year. The percent of households that received ivermectin within the community and district were compared to the 90% threshold, with coverage of at least 90% indicating programmatic success. The percent of communities that had at least 90% of households reporting to have received ivermectin was also calculated for each year. Chi-square goodness of fit tests were used to compare the percent of households receiving ivermectin and the percent of communities with at least 90% coverage in each of 2007, 2009, and 2010 to the average respective measurements for annual treatment.

Multivariate logistic regressions were then used to identify associations between CDTI programming with the failure for a household to receive ivermectin treatment[6]. Specific variables assessed related to personal involvement in CDTI and CDTI programming logistics. A separate regression was used for onchocerciasis control and elimination programs, occurring in 2004-2006 and 2007, 2009, and 2010, respectively. Regressions were also conducted for each year individually (2004, 2005, 2006, 2007, 2009, and 2010). The same variables were used in each model with the outcome differing on whether the program had the purpose of control or elimination. To assess associations present in control programs, the outcome was failure to receive one dose of ivermectin during an annual CDTI year (2004-2006). For the latter, regressions with two different outcomes were run, with the outcome being: 1) failure to receive two doses of ivermectin during a semi-annual CDTI year, and 2) failure to receive one-dose of ivermectin during a semi-annual CDTI year.

The variables that were included in the analysis were: personal involvement in deciding treatment location, personal mobilization of CDTI, personal attendance at health education sessions, providing CDD/CHW with tokens of gratitude, the location of treatment, the distance of treatment

[6] The regressions were modeled based on failure to receive treatment instead of receipt of ivermectin as the former was a rare event. The reference levels for variables in the models were chosen based on what the Carter Center and the literature perceived to be best practices in CDTI. As such, the odds ratios are a satisfactory estimate of the risk ratio, while providing valuable information on which components of CDTI are crucial to implement to avoid failure and maximize success.

from the person's household, the method by which CDD/CHW were selected, and the method by which the treatment location was decided. Personal involvement in selection of the CDD/CHW was excluded from regression models and analyzed separately because more than 10% of responses were missing for the onchocerciasis control period and more than 20% of data missing for the elimination period. The associations between variables and failure to receive treatment were descriptively compared between models.

Finally, the trends in CDTI logistics and programming between control and elimination onchocerciasis programs were analyzed descriptively over time to track the future of CDTI programming and improve upon it. These variables were aggregated and assessed at the household level, but responses for each variable were compared across communities between control and elimination programs.

Data were stored in Epi-Info and transferred to SAS 9.1 and Microsoft Excel 2007, which were used for analysis. Microsoft Excel 2007 was used to generate supporting tables and figures while ArcGIS 10 was used to create accompanying maps, unless otherwise noted.

Consent: Consent to survey households was provided orally at community meetings. Selected individuals had a right to refuse to participate in the survey without fear of repercussion. As this was part of routine program monitoring, no IRB approval was required.

Results

Objective One: Treatment Coverage

Over 90% of the approximately eleven thousand respondents reported to have received ivermectin treatment during the survey years in both control and elimination programs, but a greater percentage of respondents received treatment during the latter (Figure 3). The percent of respondents that received at least once-annual treatment significantly increased from an average of 92.29% (2004-2006) to an average of 97.13% (2007-2010) after Uganda adopted its elimination program (p<0.001). Treatment rose most dramatically between 2006 and 2007 – the start of the elimination program – with the number of respondents that reported to receive at least one treatment of ivermectin rising from 92.8% in 2006 to 98.3% in 2007 (p<0.001). The difference in treatment levels was significant but less dramatic between respondents receiving twice-annual treatment of ivermectin in the elimination period compared to respondents receiving once-annual treatment in the control period. Ninety-four percent of respondents received twice-annual ivermectin treatment (2007-2010) compared to 92.3% of households receiving once-annual treatment during the control program (p<0.001). The percent of households receiving twice-annual treatment was at its highest in 2010 (94.3%). During the elimination period, 3% fewer respondents received at least twice-annual ivermectin treatment than at least once-annual treatment, but this difference declined from 2007-2010 and was smallest in 2010 at 1.1%.

The proportion of sampled communities in which at least 90% of respondents received once-annual ivermectin treatment was significantly higher between the elimination and control campaigns, but the proportion of sampled communities in which at least 90% of respondents received twice-annual ivermectin treatment was lower in comparison to once-annual treatment (Figure 4). On average, 79.8% and 92.3% of communities in the elimination and control programs, respectively, had at least 90% of respondents who reported to receive at least once-annual ivermectin treatment (p<0.001). Contrarily, the number of communities in which at least 90% of households received two-doses of ivermectin per year was less than the proportion of communities that achieved 90% coverage under the control strategy (71.8% versus 79.8%, respectively). Similarly, during 2007-2010, although 92% of communities achieved 90% coverage of once-annual ivermectin treatment, only 72% of communities achieved 90% coverage of twice-yearly treatment.

The proportion of communities attaining 90% of treatment coverage declined from 2007 to 2010, while remaining fairly constant during the control period. The percentage of communities attaining 90% of at least once-annual treatment coverage increased dramatically between 2006 and 2007 (79.8% to 96.9%, p<0.001), but decreased to 86.0% in 2010. Similarly, for twice-annual treatment, the proportion of communities achieving at least 90% decreased steadily from 2007-2010 (75.4% in 2007, 713% in 2009, and 68.0% in 2010). 2010 was the only year in which the proportion of communities achieving 90% coverage for once-annual treatment was not significantly higher than the control period ($p=0.27$), and it was the only year in which twice-annual treatment was significantly less than once-annual treatment during the control period ($p<0.05$). As for the control period, the proportion of communities attaining 90% treatment coverage ranged from 77.8 to 80.8%.

There was a range of ivermectin treatment coverage between districts (Figure 5). During the control program, three out of seven sampled districts failed to achieve at least 90% ivermectin treatment coverage of respondents including the following: Kisoro (84.2% in 2004, 78.0% in 2005), Manafwa (88.4% in 2005), and Moyo (84.8% in 2004, 83.6% in 2005, but 96.8% in 2006). Within the elimination program, no districts failed to achieve at least 90% coverage for once-annual ivermectin treatment among respondents (Range: 94.2% to 99.6%), and only two of eight districts failed to achieve 90% twice-annual ivermectin coverage: Kamwengye (88.5% in 2007) and Hoima (85.9% in 2009). Kanungu and Mbale districts, which were sampled both during the onchocerciasis control and elimination programs saw few changes between programs.

Communities that failed to achieve 90% ivermectin coverage tended to be clustered by district and sub-district. Examining the ivermectin coverage distribution in 2009 best reveals this variation in which Bududa and Kanungu districts achieved 97.3% and 99.3% household coverage, respectively, while Hoima district achieved only 85.9% coverage. Within Bududa and Kanungu, only 12% (3 of 25) and 4% (1 of 25) of communities failed to achieve 90% ivermectin treatment coverage, respectively, while in Hoima, 43% of communities failed to achieve 90% coverage. Within the six sub-districts sampled in Hoima, four had household ivermectin coverage rates that were $<90\%$. However, even within sub-district that failed to achieve adequate coverage, there was wide variability of coverage between communities. For example, the Kigorobya sub-district of Hoima had 83.8% household ivermectin coverage, but two of its six sampled communities achieved only 44.8% and

60.7% coverage. Contrarily, the Kitoba sub-district in Hoima, which also failed to achieve 90% coverage, had seven of its ten sampled communities that did not obtain 90% coverage.

Objective Two: Associations between CDTI variables and receipt of ivermectin

Multivariate logistic regressions between CDTI programming variables and receipt of ivermectin revealed that failure to be personally invested in CDTI activities was strongly associated with failure to receive a single treatment of ivermectin annually during control and elimination programs, but it was much more minimally associated with failure to receive twice-annual treatments in the elimination program (Tables 2 and 3). The most pronounced association existed between attendance at health education sessions and receipt of ivermectin. Households that failed to attend health education sessions were on average approximately 1.9 times more likely to not receive two-doses of treatment per year than households that attended health education sessions ($p<0.001$). However, households were 3.5 and 2.9 times more likely to not receive at least a single dose of treatment under control and elimination programs, respectively ($p<0.001$). A similar association was evident for each year of CDTI separately. There was also a significant association between personal involvement in deciding treatment location and receipt of one-dose of ivermectin per year. The respondents that were not involved in deciding treatment location were approximately 45% and 29% more likely to not receive treatment during control and elimination programs, respectively, than households involved in this decision ($p<0.05$ and $p=0.41$, respectively). Conversely, persons not involved in deciding where treatment occurred had greater odds of receiving two doses of ivermectin per year ($p=0.12$). Similar associations were found for personal involvement in mobilization of CDTI activities. Not being involved with CDTI mobilization efforts was found to increase the odds of not receiving twice-annual treatment of ivermectin by 39% ($p<0.05$), but it increased the odds of not receiving any treatment by approximately 52% and 82% in control and elimination campaigns, respectively ($p<0.01$). However, this association was highly variable between years (Table 3). For example, the association between involvement in CDTI mobilization and receipt of ivermectin was much higher in 2009 than it was in 2007 or 2010 for both one and two-doses of ivermectin (3.18 versus 1.04 and 1.49 times higher, and 2.02 versus 0.86 and 1.24 times higher, respectively). Regardless, for each year the association between CDTI program variables and failure to receive at least one-dose of ivermectin was always stronger than it was with failure to receive two-doses of ivermectin.

The location of treatment and community-based participation in choosing this location were found to be most strongly and consistently associated with twice-annual treatment. Overall, the failure to involve the kinship unit to decide upon the location of treatment was associated with failure to receive twice-annual ivermectin treatment but not once-annual treatment. In 2007 and 2009, respondents that stated their kinship unit was not involved with deciding treatment location had 3.8 and 2.2 times greater odds of failing to receive twice-annual treatment, respectively ($p<0.05$). That is, if treatment location was decided by the CHW/CDD, at a general community meeting outside the kinship unit, or by the community-directed health supervisor, the odds of failure to receive two doses of ivermectin increased compared to when this decision with the kinship unit. Similar but weaker and insignificant relationships were found for failure to receive once-annual treatment in the elimination program. Similarly, for each year of CDTI in this study, if treatment location did not occur in a respondent's house/compound, he/she was significantly more likely to not have received treatment ($p<0.05$). Treatment location did have a stronger impact on failure to receive at least once-annual treatment in the control and elimination programs than twice-annual treatment but was still very strong for twice-annual treatment (Figure 3). From 2007-2010, respondents who did not have access to treatment at their home/compound had 2.1, 2.0, and 2.7-times greater odds of not receiving twice-annual treatment ($p<0.05$).

Point estimates also suggest that failure to select CDD through community meetings is associated with failure to receive ivermectin, but this association was not consistent across the years and generally lacked statistical significance (Tables 2 and 3). However, in onchocerciasis control and elimination programs persons citing no personal involvement in distributor selection[7] were found to be 3.6 and 4.1 times significantly more likely to not receive once-annual treatment of ivermectin than persons involved in distributor selection, respectively ($p<0.001$). This association was weaker but still significant for receiving two-doses of ivermectin per year, as persons not involved in distributor selection had 2.2 times greater odds of to not receiving treatment twice-yearly ($p<0.001$). Similarly, there was a significant association between households not knowing how CDD were selected in comparison to CDD being selected by community members at a public meeting and failure to receive two-doses of treatment ($p<0.001$).

Finally, there were no consistent associations between households providing gifts to CDD and receipt of ivermectin treatment for control or elimination (Tables 2 and 3). In some years, specifically for twice-annual treatment of ivermectin in 2007 and 2010, provision of gifts was negatively associated with obtaining sufficient treatment. However, in 2006 and 2009 the data suggest that not providing tokens of gratitude to ivermectin distributors was significantly associated with failure to receive treatment.

Objective Three: Trends in CDTI Programming

Analyzing CDTI programming as reported by respondents revealed significant changes in CDTI implementation between onchocerciasis control and elimination programs.[8] Personal involvement in CDTI during the elimination program fluctuated widely, whereas it remained fairly constant from 2004-2006 (Figure 6). For example, personal involvement in deciding upon treatment location remained steady from 2004- 2006, with approximately two-thirds of households reporting to be involved in making this decision. However, from 2007 to 2009, this number dropped from approximately 65% to 40% and continued to decrease in 2010. There was a similar yet less dramatic decrease in personal involvement with the mobilization of CDTI activities. During the years of

[7] There were large numbers of missing data for this variable. In total, 492 data points were missing for this question on annual surveys and 1,224 from semi-annual.
[8] Due to the high numbers of households sampled, all differences between the average annual CDTI percentages and those from each semi-annual year were statistically significant. As such, the extent of these differences was more important to assess than significance.

onchocerciasis control, two-thirds of people were involved with mobilization of the CDTI campaigns. However, with the advent of elimination program, there was a 5% decrease in this involvement, which continued to decrease to 58.5% in 2010 from approximately 70% in 2005. Change in personal involvement in distributor selection[9] followed a similar trend, but there was one substantial difference. From 2006 to 2007, the percentage of households involved with distributor selection increased from 77% to 92.4%, but then rapidly plummeted so that by 2010 involvement was 11% under the average from the onchocerciasis control program years. Conversely, although personal attendance at health education sessions fluctuated, attendance rates were highest in 2010. The percent of households that reported giving something to the CDD also increased sharply during the elimination period, rising from 9.5% in 2009 to 20.3% in 2010 alone. Overall, at the end of the onchocerciasis elimination study period, households were less involved in deciding treatment location, mobilizing CDTI campaigns, and selecting distributors, but more prone to attend health education sessions and provide gifts to the community distributors.

In assessing other program variables of CDTI, the onchocerciasis elimination program when compared to the control program was found to provide greater convenience to ivermectin treatment but be less rooted in community-based principles (Figure 7). On average, the elimination program increased the percentage of households reporting to have received ivermectin treatment at their own home by 40%, and as a result the percentage of households reporting treatment to have occurred less than 0.5 km from their house increased 20 percentage-points. However, from 2009 to 2010, the percent of people receiving ivermectin treatment in their homes decreased from almost 90% to less than 70%. The distance of treatment from home also decreased but not to the same extent (97.1% to 91.3%).

Conversely, the reliance upon community engagement in the CDTI process decreased during the elimination campaign. In the control program, between 55-60% of households reported that decisions regarding treatment location occurred within the kinship structure, a number that

[9] There were large numbers of missing data for this variable. In total, 492 data points were missing for this question on annual surveys and 1,224 from semi-annual.

remained constant from 2004-2006. However, from 2007 to 2010, the percent of households reporting that the kinship unit or neighborhood decided upon treatment location steadily declined, with only 35.9% of households stating the involvement of the kinship unit in 2010, 23% lower than the control program average. Similarly, the process by which CDD were selected showed decreased involvement of community members. Although there was a rapid increase in community members selecting distributors at the start of the evaluation campaign, this involvement quickly dwindled. By 2010, only 61% of respondents reported that community members selected CDD. Although this figure was higher than the 2006 level, the elimination program average was approximately 10% lower than the control program average. Overall, 21% of households stated they did not know how community distributors were selected for CDTI under the elimination program, in comparison to 14% during the control program. Similarly, 5% of households reported that community leaders appointed the CDD in the elimination program versus 3% of households in the control program.

Community-level and District-level Analysis

CDTI programming was highly varied between communities and districts. The percentage of households per community expressing involvement with CDTI[10] and stating CDTI processes were more convenient[11] and community-oriented[12] were non-normally distributed in both the control and elimination programs. The most variability existed in the years under the elimination program. Factors related to location of CDTI, including the agents involved in choosing location, had especially wide variability between communities. Similarly, between districts the percent of households involved in deciding treatment location varied widely, ranging in 2004 alone from 49% in Kisoro district to 77% in Kannungu district. Certain districts, specifically Hoima, tended to have lower overall achievement of the desired logistical components of CDTI (i.e. household and community-level involvement in the CDTI process). However, each district generally demonstrated a balance of strengths and weaknesses in achieving preferred CDTI procedures.

[10] This includes: households personally helped decided upon treatment location, helped mobilize CDTI activities, participation in the selection of distributors, attended health educations sessions, and/or gave gifts to CDD/CHW for their CDTI services

[11] This includes: treatment location was less than 0.5km from household, treatment occurred a person's house/compound

[12] This includes: kinship/neighborhood decided treatment location, community members selected distributors

Satisfaction with Services

Regardless of differences in treatment convenience, personal involvement, or community engagement in CDTI planning, satisfaction with services remained above 90% from 2004-2010 (Figure 7). Personal satisfaction did experience a 5% increase at the start of the onchocerciasis elimination program (2007), where it reached its maximum of 98% of respondents expressing satisfaction with CDTI services. However, this level fell to 91.5% in 2010, the minimum percent of persons expressing satisfaction with services in this study period. Nonetheless, the respondents' expressed intent to return for treatment in the following year remained constant from 2004 – 2010, the only variable for which there were no significant differences noted between annual and semi-annual years.

Discussion

Uganda has proven the tremendous capacity of its community-based efforts to battle onchocerciasis by demonstrating the success of its onchocerciasis elimination program, in which more than 90% of respondents obtained twice-annual ivermectin treatment through semi-annual CDTI. The elimination program was overall more successful than the control program, as it significantly raised the coverage of eligible individuals for both once-annual and twice-annual treatment with ivermectin. The CDTI campaigns in the elimination program also raised the percentage of communities that achieved at least 90% ivermectin coverage. This suggests that the semi-annual CDTI campaigns implemented during the elimination program have greatly increased ivermectin distribution and ivermectin coverage so that better control is established. That is, regardless of success in elimination, increased CDTI campaigns have succeeded in reaching increased numbers of households to increase impact of onchocerciasis control and treatment. Moreover, the success of the elimination program in comparison to the control program disproves the claim that communities may find it more difficult to maintain high performance of CDTI under the elimination strategy.

However, more work needs to be done to ensure all communities have sustained access to twice-annual treatment. The percentage of communities achieving at least 90% once-annual and twice-annual ivermectin coverage has declined since the initiation of the program. The percentage of communities achieving success in twice-annual ivermectin coverage is especially low, suggesting that resources and training need to be reassessed at the community level. As attainment of at least 90% ivermectin coverage was consistent and more pronounced in districts where community members have traditionally been more involved in decision making and involvement in program activities, this study confirms past evaluations that suggest communities need to be mobilized, educated and involved with CDTI to increase coverage evaluations (Katabarwa, et al 2000, Katabarwa et al 2001, Katabarwa et al 2001-b, Katabarwa 2002; Katabarwa et al 2002b, Katabarwa et al 2005, Katabarwa 2010-b, Katabarwa, Habomugisha, and Richards 2000). The overall decrease in community participation in CDTI programming from 2007-2010 reveals potential instability to the elimination program.

Achieving further success in twice-annual ivermectin treatment coverage could require slightly different tactics, though, than those used to achieve success for once-annual treatment. Although changing the onchocerciasis programs from control to elimination, and subsequently annual to semi-annual CDTI, did not greatly affect the association between CDTI program variables and receipt of once-annual ivermectin coverage, there were different associations observed between CDTI program variables and receipt of twice-annual ivermectin. Specifically, the involvement of the kinship unit involvement was found to be substantially more associated with receipt of two annual doses of ivermectin per year than once-annual treatment. This is likely the cause for the Hoima district's failure to achieve 90% twice-annual ivermectin coverage in 2009, as the district was one of the last to embrace the kinship-enhanced CDTI approach. Receiving treatment at one's house/compound was similarly associated with receipt of twice-annual treatment. Equally important to note is that a weak or no association existed with twice-annual treatment and many variables that were strongly associated with receipt of once-annual treatment, such as personal involvement in

CDTI activities, like health education, CDTI mobilization, and choosing treatment location. This suggests that although individual involvement in CDTI remains important as it does continue to be associated with receiving ivermectin treatment, successfully increasing twice-annual treatment coverage will require increased consideration of the kinship unit and consideration of factors outside the basic CDTI model.

These associations are important to consider when assessing the trends in CDTI programming over time. Based on associations seen between CDTI variables and ivermectin receipt, the overall decrease in personal investment in CDTI during the elimination program does not necessarily bode poorly for the elimination program. The drastic increase in persons receiving treatment closer to one's home between control and elimination programs suggests that CDTI is functioning in a manner that could naturally increase the percentage of households receiving twice-annual treatment with ivermectin. However, the dramatic drop in variables of community involvement with CDTI that are associated with receipt of ivermectin, specifically community selection of the CDD and kinship unit involvement, suggests that there could be problems retaining the high levels of ivermectin coverage that were observed to date in this study. Similarly, an increased rate of gift giving, a factor that has been negatively associated with ivermectin coverage, accompanies these changes, which suggests that steps may need to be taken to reorient CDTI to the community.

The Impact of Exterior Factors

As factors related to CDTI programming were generally more strongly associated with receiving once-annual ivermectin treatment than twice-annual treatment, factors extraneous to CDTI need to be investigated to better understand what is impacting successful onchocerciasis elimination (at least twice-annual ivermectin treatment) in Uganda. There are many such factors that likely impacted the success of ivermectin coverage that were not investigated in this study, specifically CHW and CDD involvement in the communities.

Throughout the timeframe in this study, there were frequent transfers of CHW from endemic onchocerciasis areas to non-endemic areas. This created a large influx of untrained CHW into onchocerciasis endemic areas, which meant workers lacking knowledge on or practice of CDTI were left to organize CDTI processes, including the training of CDD. Frequent redistricting of communities, sub-districts, and districts to smaller units increased this problem, as new political borders increased the number of health workers that were required. This likely further increased the numbers of under-skilled CHW to organize CDTI, which could have diminished the program capacity. Moreover, high attrition at the national level (e.g., the coordinators for the National Onchocerciasis Program changed three times from 2008-2009) could have impacted the overall support and guidance provided to the local level. Finally, in 2010, there were other short-lived community-based health programs in some districts that did not incorporate CDTI. This could have impacted participation in the CDTI processes in 2010 by over burdening community members.

Regardless of changes in the CDTI process or participation in CDTI between elimination and control programs, the households almost unanimously expressed satisfaction with CDTI and a willingness to return in the following year for treatment. This suggests that CDTI is becoming increasingly engrained in the communities and remains fully accepted, if not expected, by households. The community's long-term engagement with CDTI has the potential of decreasing involvement with and increasing complacency toward the program. Although this has not negatively impacted ivermectin coverage to date, research continues to suggest that community involvement in the CDTI process is essential for ensuring successful programs (Katabarwa et al 1999; Katabarwa, et al 2002; Katabarwa et al 2005). As such, it remains advisable to continue to maximize community engagement in CDTI processes, but to investigate what extrinsic factors are responsible for differences in successfully achieving once-annual treatment versus twice-annual treatment.

Limitations

Despite the robustness of this data, there are many limitations to this study that hinder a complete analysis of Uganda's CDTI approach for its onchocerciasis elimination program. Firstly, a rigorous evaluation could not be completed because there is little comparison data available. There were no appropriate comparison groups that could be used to isolate the CDTI program because the same communities were not measured repeatedly through the years and control and elimination programs were not implemented in the same time frame. As CDTI data from onchocerciasis control and elimination programs were not available for the same time period, external difficulties known to impact the success of CDTI, such as weather events and political instability (Katabarwa, et al 1999) could not be accounted for in this study.

Likewise, this study was unable to analyze socioeconomic factors in relation to success of CDTI. Information on household socioeconomic status was not gathered through the survey instruments and was subsequently unavailable for analysis. Information on road coverage, development indexes, and overall infrastructure were also unavailable at the community level. As a result, systematic differences could not be accounted for between communities sampled in the onchocerciasis control and elimination years. Disaggregating data by district and in some cases, sub-district, showed that there were substantial differences in CDTI programs and success between district and sub-district, but the lack of socioeconomic data and other external data (e.g., attrition rates of CHW or CHW involvement in the community) hindered elucidating reasons for these differences. As a result, this study was only able to analyze CDTI programs and associations between success or failure to receive ivermectin and the various CDTI components.

The study design also possesses limitations to the generalizability of this analysis. As data was collected in a multi-stage random sampling framework from relatively few primary sampling units (e.g., three districts per year), healthy skepticism must be maintained when considering the results in relation to all districts of Uganda. The disaggregated data suggest that CDTI programming and success can vary widely between districts so an analysis of three districts may be insufficient to draw conclusions for the entire country. Nonetheless, random sampling ensures that the data can provide excellent information on associations between CDTI components and program success.

Finally, the assessment of the chemical and physiological effectiveness of CDTI in the elimination program was outside the scope of this study. No data is available at this time to evaluate the effectiveness of the semi-annual ivermectin distribution strategy to feasibly eliminate onchocerciasis in endemic areas of Uganda.

Programming Implications and Future Research

Although there are limitations to this study, the analysis provide an excellent framework for Uganda to critically examine its strategies for onchocerciasis elimination and bolster success by illuminating factors that need to be addressed to sustain and improve receipt of ivermectin twice-annually. Firstly, the steep increase in community-level participation for CDTI in 2007 followed by rapid decline in involvement suggests that Uganda's renewed enthusiasm for the fight against onchocerciasis was short-lived. It appears that communities, and subsequently CDD/CHW, may be becoming fatigued, or perhaps complacent, on issues regarding onchocerciasis, and as such, creating sustained enthusiasm for an even greater frequency of ivermectin treatment may be challenging. This has the possibility of decreasing the percentage of households that take ivermectin if appropriate measures are not implemented. However, this study shows that although community participation in CDTI is important, individual participation in CDTI planning and implementation may not be essential for long-term ivermectin distribution. If the community becomes fatigued, perhaps time can be better allocated by focusing on select leaders in the kinship unit to help make programmatic decisions in a representative fashion and maintain awareness among their familial unit.

It would be wise to also re-examine the allocation of resources (e.g., ivermectin, CHW) to ensure that the number of people receiving ivermectin in close proximity to their home and the involvement of the kinship unit is maximized in all communities. Overall, the elimination programs were able to increase the number of people receiving ivermectin in close proximity to their house from control CDTI levels, but this number dropped sharply in 2010. Similarly, the reliance on the kinship unit to decide the place of treatment steadily declined with the start of semi-annual CDTI. Both of these observations are problematic because failure to provide treatment at a person's home increases the odds that they will fail to receive any ivermectin treatment by up to six-fold and the odds that they will fail to receive twice-annual ivermectin treatment by approximately two-fold. Similarly, as failure to include kinship in deciding upon the place of treatment is associated with failure to receive ivermectin treatment, specifically twice-annual receipt of ivermectin, the sustained decline in involvement of kinship could hinder elimination. Failure to provide treatment at home under the kinship model also has the possibility of decreasing women's access to ivermectin treatment (Katabarwa, et al 2010-b; Katabarwa, et al 2002-b). As such, strategies need to be employed that increase use of the kinship system in CDTI, particularly to continue to make the place of treatment more convenient. As coordination with the kinship unit is known to be paramount to achieving long-lasting CDTI success in Uganda (Katabarwa, et al 2010-b), special emphasis needs to be placed on renewing efforts to mobilize the community through the kinship structure.

In addition, Uganda should investigate community-level differences, including socioeconomic, political, and/or structural, and their association with the community's ability to achieve 90% ivermectin coverage. In this study, the percentage of communities with at least 90% of respondents receiving twice-annual doses of ivermectin was significantly lower than ivermectin coverage under the control program, and this difference was apparent at the community level but not at the individual respondent level. This suggests that barriers to receiving ivermectin exist at the community level that are different than those at the individual level and need to be understood to achieve sustained success in Uganda's onchocerciasis elimination program.

This study also suggests that further operational research needs to be conducted to understand what level of community involvement is required to ensure prolonged success in onchocerciasis elimination programs. As ivermectin becomes increasingly engrained in the culture of a community, this study has found varying levels of community participation in CDTI but consistent success and satisfaction with services. Quality studies need to assess if this decline in communal participation in CDTI organization is harmful to program success considering the community's longstanding history with CDTI. Improving our understanding on the degree to which community participation remains relevant will ensure that resources are properly allocated to maximize success in onchocerciasis elimination programs.

Finally, there remains much to be analyzed regarding the feasibility of achieving onchocerciasis elimination through semi-annual CDTI in endemic areas in Africa. Further research needs to be conducted on the long-term physical effectiveness of ivermectin treatment under semi-annual CDTI in comparison to annual CDTI. This could be done by implementing robust evaluations with relevant comparison groups, preferably using standard double-difference techniques or randomized control trials, to understand differences between onchocerciasis control and elimination campaigns.

Conclusion

Onchocerciasis elimination programs in Uganda can be implemented as successfully, if not more successfully, than control programs through semi-annual CDTI, but strategic efforts must be considered to strengthen the community-based processes of CDTI and community-engagement with CDTI to maximize sustained high ivermectin coverage. Bolstering standard community-level participation in CDTI is not likely to increase coverage of twice-annual ivermectin treatment as this study suggests that CDTI factors alone cannot explain receipt of twice-annual treatment of ivermectin. Within the CDTI framework, specific variables, such as the kinship unit and location of treatment, should be used to improve twice-annual treatment coverage. Moreover, the role of individuals in CDTI processes needs to be reexamined as high treatment rates endure despite decreased communal processes of CDTI. Ultimately, factors extrinsic to community-based participation in CDTI must be further investigated to understand how Uganda can strengthen its national onchocerciasis elimination program.

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Figures

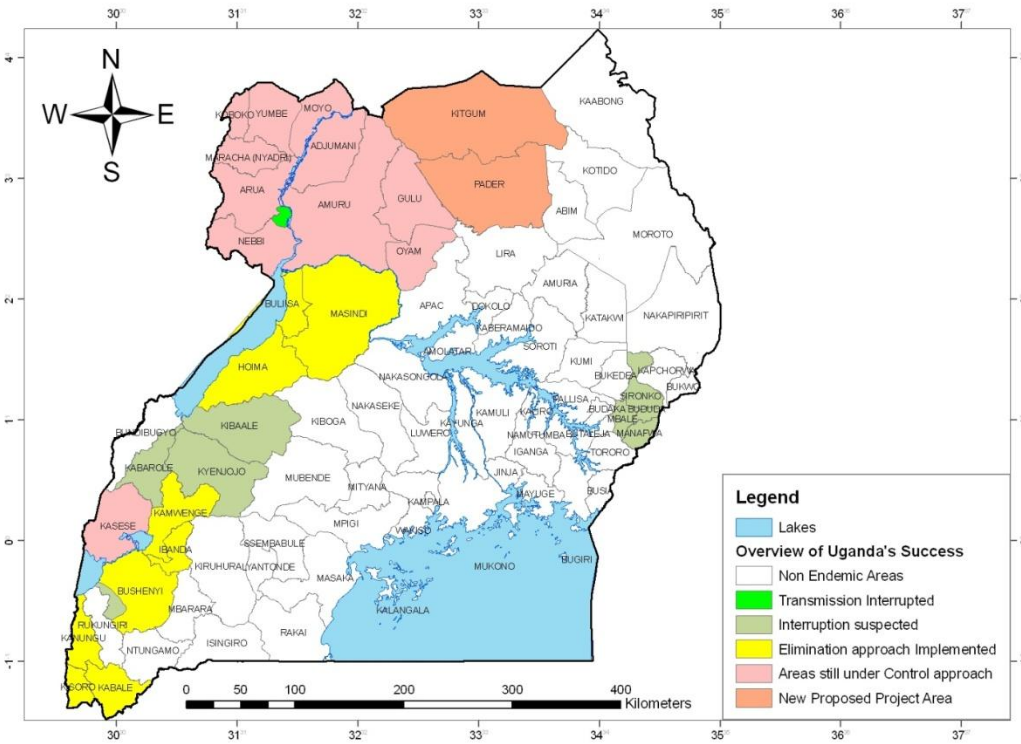

Figure 1. Onchocerciasis elimination programs in Uganda as of 2008. *Map provided for inclusion in this report by field advisor at the Carter Center.*

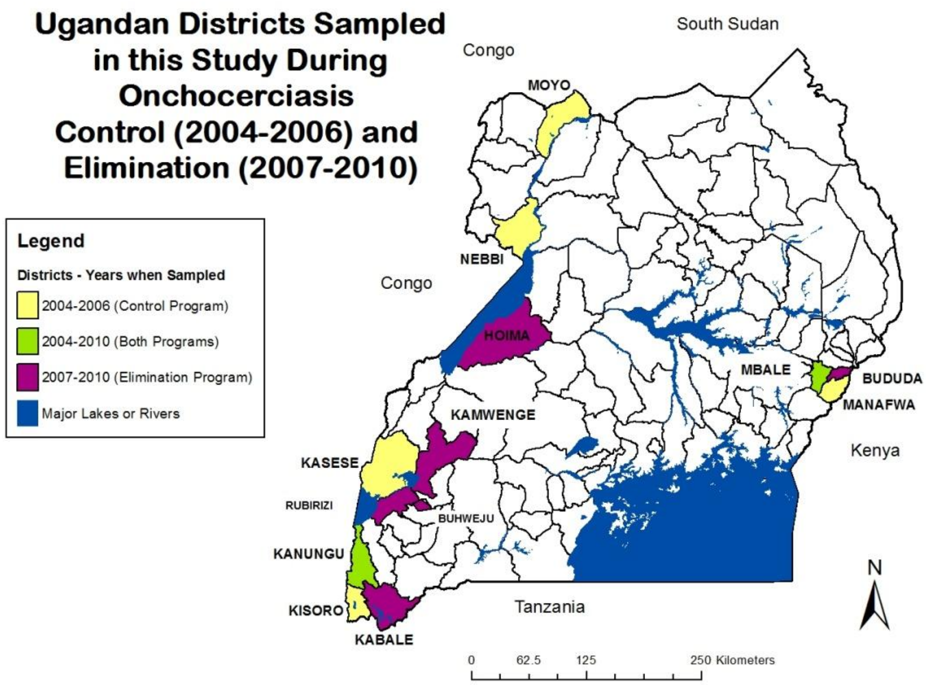

Figure 2. Districts sampled during Uganda's Onchocerciasis Control and Elimination Programs in 2004-2006 and 2007-2010, respectively. *The following districts were sampled each year: 2004 – Kanungu, Kisoro, Mbale, Moyo, and Nebbi; 2005 – Kanungu, Kasesse, Kisoro, Mbale, and Moyo; 2006 – Kisoro, Manafwa, Moyo, and Nebbi; 2007 – Kamwengye, Kanungu, and Mbale; 2009 – Bududa, Hoima, and Kanungu; and 2010 – Buhweju, Kabale, and Rubirizi.*

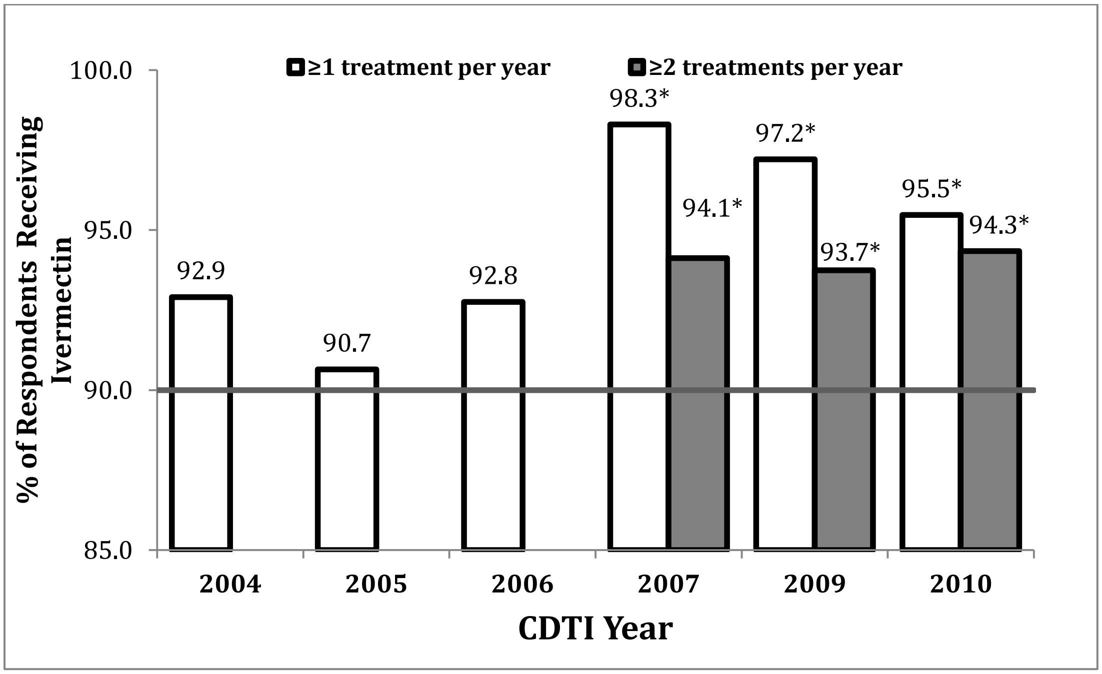

Figure 3. Percent of Respondents Reporting to have Received Ivermectin in the given year, with 90% being the threshold for CDTI success. **Indicates a significant difference exists between this measurement and the average treatment coverage for 2004-2006.*

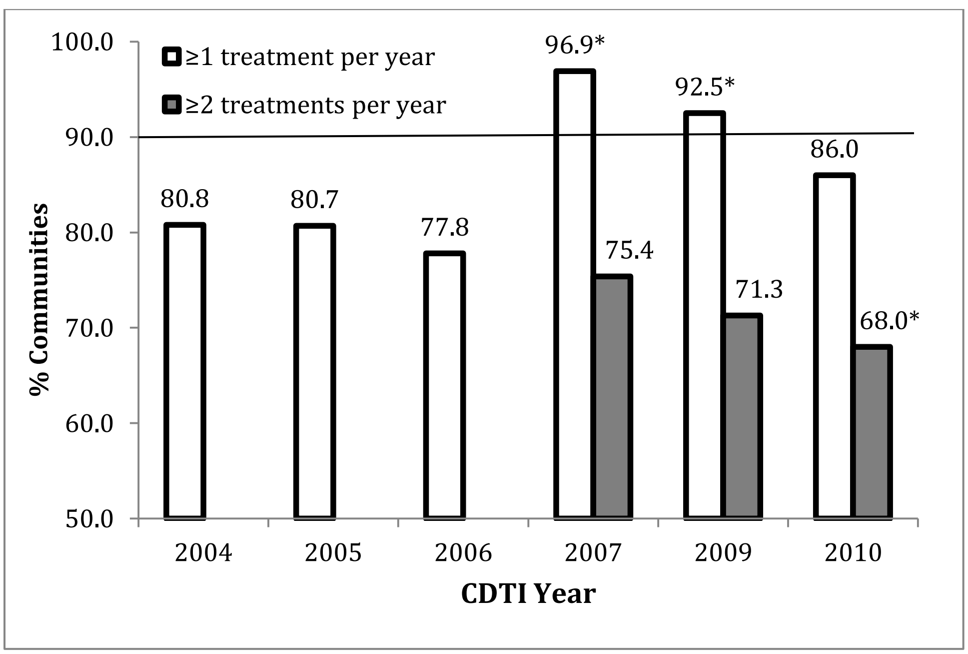

Figure 4. The Percent of Communities that achieved at least 90% ivermectin coverage among respondents in the given CDTI year. **Indicates a significant difference exists between this measurement and the average percent of communities with at least 90% treatment coverage for 2004-2006.*

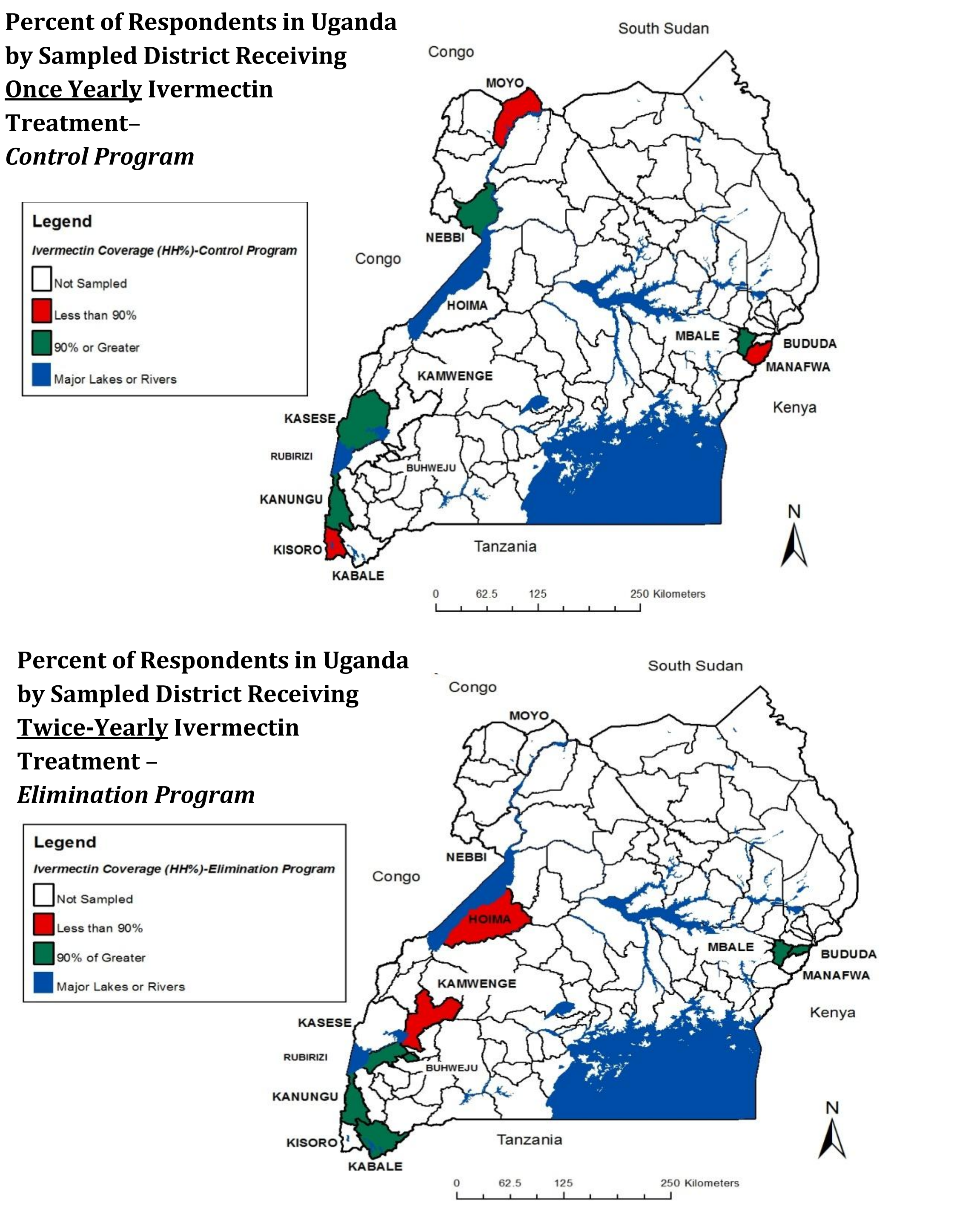

Figure 5. Percent of respondents receiving once-annual and twice-annual ivermectin treatment in sampled districts during control and elimination programs, respectively.

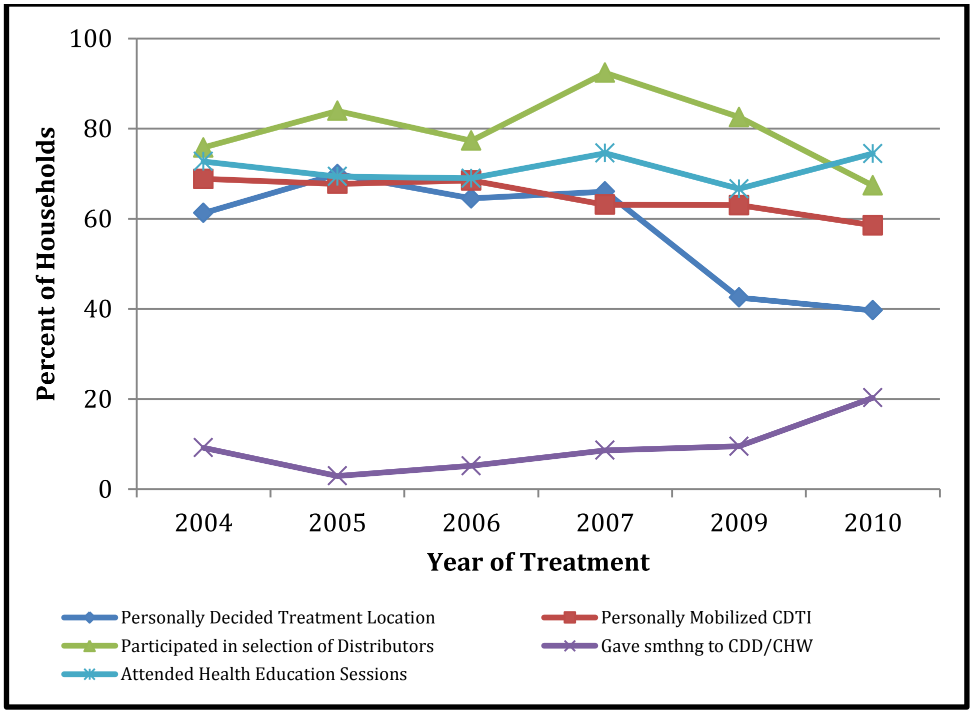

Figure 6. The percent of sampled respondents involved in various aspects of CDTI programming by year.

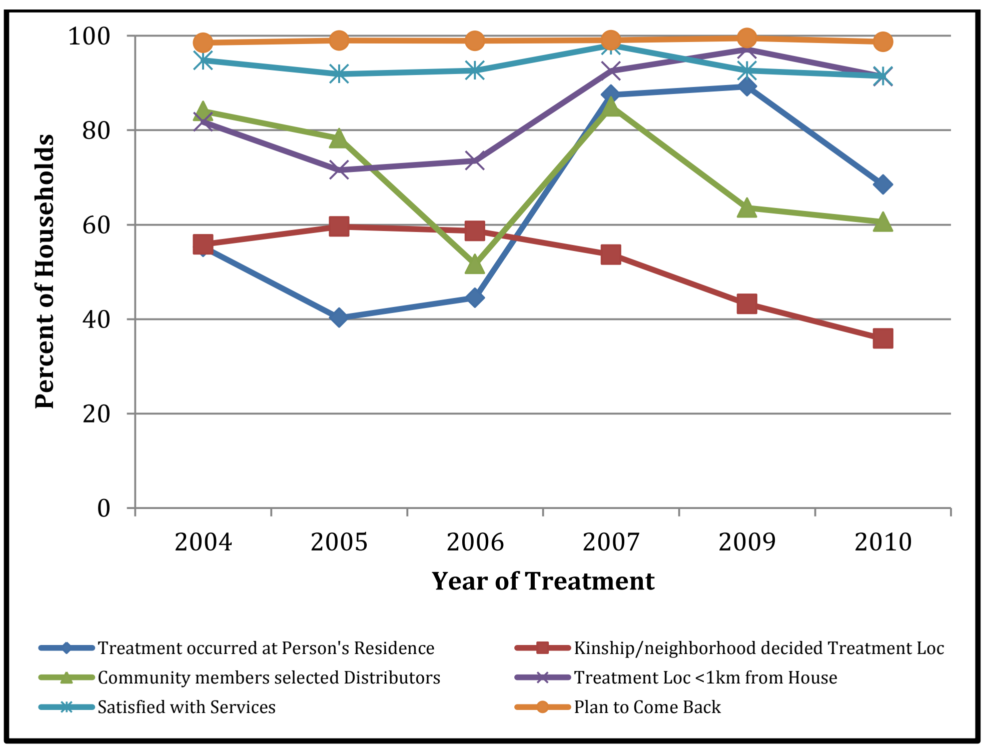

Figure 7. CDTI Programming Logistics and Recipient Satisfaction from 2004-2010 as expressed by sampled respondents.

Tables

Table 1. The number of districts, health areas, communities, and respondents surveyed each year.

Survey Year	Districts (Sub-regions)	Health Areas (Sub-areas)	Communities	No of Respondents
2004	5	33	112	1,100
2005	5	33	112	1,200
2006	4	24	89	2,696
Control Total	**14 (Total) 7 (Unique)**	**90**	**313**	**4,996**
2007	3	13	68	1,946
2009	3	18	80	2,400
2010	3	8	50	1,500
Elimination Total	**9 (Total) 8 (Unique)**	**39**	**198**	**5,847**

Note: Some districts were surveyed in multiple years. For districts, 'total' refers to the total number of districts sampled over the specified years, while 'unique' refers to how many different districts were sampled over the specified years. Health areas and communities may also have been sampled in multiple years, but these numbers were not disaggregated.

Table 2. The association between CDTI programming variables and failure to receive ≥1 or ≥2 ivermectin treatments per year under Uganda's Onchocerciasis Control or Elimination Programs (2004-2006 and 2007-2010, respectively). * Indicates significance at the 95% confidence level.

	Control Program		**Elimination Program**			
Failure to Receive:	**≥1 treatment / year**		**≥1 treatment / year**		**≥2 treatments / year**	
CDTI Variables	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**
Location of Treatment						
My house/compound	2284 (45.8)	1.0	4872 (83.3)	1.0	4872 (83.3)	1.0
Community center	1942 (38.9)	1.60 (1.17, 2.20)*	644 (11.0)	1.365 (0.77, 2.43)	644 (11.0)	1.84 (1.23, 2.75)*
Community Leaders compound	241 (4.8)	1.07 (0.60, 1.93)	133 (2.3)	2.11 (0.92, 4.87)	133 (2.3)	3.83 (2.05, 7.13)*
Health Unit	5 (0.1)	0.78 (0.05, 12.0)	0 (0)	--------	0 (0)	-------------
CDHW's home	433 (8.7)	2.08 (1.39, 3.12)*	141 (2.4)	3.47 (1.63, 7.39)*	141 (2.4)	2.15 (1.13, 4.06)*
I don't know	82 (1.6)	27.7 (14.1, 53.9)*	56 (1.0)	36.58 (16.8, 79.6)*	56 (1.0)	5.07 (1.75, 14.7)*
Involved in deciding treatment location						
Yes	3240 (65.1)	1.0	2899 (49.6)	1.0	2899 (49.6)	1.0
No	1737 (34.9)	1.45 (1.02, 2.08)*	2945 (50.4)	1.285 (0.71, 2.34)	2945 (50.4)	0.73 (0.49, 1.08)
Involved in CDTI mobilization						
Yes	3400 (68.4)	1.0	3612 (61.9)	1.0	3612 (61.9)	1.0
No	1571 (31.6)	1.52 (1.14, 2.01)*	2224 (38.1)	1.82 (1.16, 2.85)*	2224 (38.1)	1.39 (1.04, 1.85)*
Attended Health Education Sessions						
Yes	3487 (69.9)	1.0	4350 (74.6)	1.0	4350 (74.6)	1.0
No	1501 (30.1)	3.46 (2.61, 4.57)*	1485 (25.4)	2.88 (1.90, 4.34)*	1485 (25.4)	1.92 (1.45, 2.54)*
Distance of Treatment from Home						
Less 0.5 km	3732 (74.9)	1.0	5478 (94.1)	1.0	5478 (94.1)	1.0
≥0.5km but <1 km	986 (19.8)	1.43 (1.06, 1.94)*	310 (5.3)	1.30 (0.65, 2.59)	310 (5.3)	0.43 (0.23, 0.81)
≥ 1 km	266 (5.3)	1.77 (1.09, 2.87)*	33 (0.6)	1.38 (0.29, 6.58)	33 (0.6)	0.42 (0.093, 1.92)

Table 2 – Continued. The association between CDTI programming variables and failure to receive ≥1 or ≥2 ivermectin treatments per year under Uganda's Onchocerciasis Control or Elimination Programs (2004-2006 and 2007-2010, respectively).
* Indicates significance at the 95% confidence level.

	Control Program		**Elimination Program**			
Failure to Receive:	**≥1 treatment / year**		**≥1 treatment / year**		**≥2 treatments / year**	
CDTI Variables	**n (%)**	**OR (95% CI)**	**n (%)**	**OR (95% CI)**	**n(%)**	**OR (95% CI)**
Agent Deciding Place of Treatment						
Community meeting in kinship zone	2907 (58.3)	1.0	2619 (44.8)	1.0	2619 (44.8)	1.0
Community leader(s)	624 (12.5)	1.07 (0.71, 1.63)	608 (10.4)	1.43 (0.77, 2.65)	608 (10.4)	1.50 (0.94, 2.40)
CDHW (Distributor)	637 (12.8)	0.88 (0.57, 1.37)	956 (16.3)	0.71 (0.35, 1.44)	956 (16.3)	1.89 (1.23, 2.90)*
Community meeting outside kinship	136 (2.7)	0.53 (0.19, 1.48)	202 (3.5)	1.11 (0.38, 3.24)	202 (3.5)	2.26 (1.23, 4.13)*
Community-directed health supervisor	163 (3.3)	0.98 (0.51, 1.90)	351 (6.0)	0.90 (0.38, 2.14)	351 (6.0)	3.74 (2.30, 6.06)*
Frontline health workers	28 (0.5)	0.79 (0.19, 3.28)	207 (3.5)	0.001 (<0.01, >999)	207 (3.5)	0.26 (0.069, 1.13)
Did not know	494 (9.9)	1.01 (0.64, 1.60)	903 (15.5)	1.66 (0.84, 3.24)	903 (15.5)	1.54 (0.96, 2.49)
How Distributors were Selected						
Community members with or without leaders at a meeting	3942 (79.3)	1.0	4078 (69.9)	1.0	4078 (69.9)	1.0
Appointed by community leaders	152 (3.1)	0.61 (0.29, 1.28)	273 (4.7)	0.85 (0.37, 1.91)	273 (4.7)	1.37 (0.77, 2.44)
Self-appointed	40 (0.8)	0.65 (0.19, 2.24)	13 (0.2)	1.40 (0.07, 28.0)	13 (0.2)	0.001 <0.01, >999)
Believes appointed by community-directed health supervisor.	119 (2.4)	0.71 (0.30, 1.70)	198 (3.4)	0.99 (0.34, 2.50)	198 (3.4)	0.78 (0.39, 1.59)
Appointed by frontline health workers.	26 (0.5)	11.8 (4.85, 28.7)*	30 (0.5)	0.001 (<0.01, >999)	30 (0.5)	1.35 (0.29, 6.27)
Did not know/Other	692 (13.9)	1.38 (0.97, 1.97)	1241 (21.3)	0.73 (0.42, 1.25)	1241 (21.3)	2.19 (1.52, 3.15)*
Gave Something to Distributors						
Yes	274 (5.5)	1.0	699 (12.0)	1.0	699 (12.0)	1.0
No	4690 (94.5)	0.90 (0.46, 1.76)	5138 (88.0)	1.19 (0.68, 2.08)	5138 (88.0)	0.92 (0.62, 1.35)

Table 3. The association between CDTI programming variables and failure to receive ≥1 or ≥2 treatments of ivermectin in 2004, 2005, 2006, 2007, 2009, and 2010, expressed by Odds Ratios (95% CI)^.

	Control Program			Elimination Program					
Failure to Receive:	≥1 treatment / year						≥2 treatments / year		
CDTI Programming Variable	**2004**	**2005**	**2006**	**2007**	**2009**	**2010**	**2007**	**2009**	**2010**
Treatment Location was not at Respondent's House/Compound	3.23 (1.81 - 5.79)*	2.35 (1.41-3.91)*	2.26 (1.54-3.31)*	6.82 (2.58-18.1)*	3.50 (1.79-6.86)*	2.67 (1.50-4.73*)	2.07 (1.05, 4.07)*	1.97 (1.14, 3.41)*	2.68 (1.59, 4.52)*
Not Personally involved in deciding treatment location	2.05 (0.88-4.75)	1.74 (0.97-3.12)	1.59 (1.00-2.54)	1.08 (0.35-3.36)	0.75 (0.24-2.34)	1.83 (0.87 - 3.84)	0.22 (0.12, 0.39)*	0.81 (0.37, 1.75)	3.59 (1.68, 7.67)*
Not Personally involved in mobilization for CDTI	1.23 (0.69-2.19)	2.03 (1.22-3.37)*	1.94 (1.33-2.84) *	1.04 (0.42-2.61)	3.18 (1.55-6.53)*	1.49 (0.79-2.81)	0.86 (0.51, 1.45)	2.02 (1.32, 3.09)*	1.24 (0.70, 2.18)
Did Not Attend Health Education Sessions	8.33 (4.47-15.5)*	2.25 (1.42-3.55)*	3.86 (2.63-5.67)*	2.83 (1.09-7.33)*	1.95 (1.01 - 3.79)*	4.67 (2.64-8.26*)	2.24 (1.30, 3.86)*	2.45 (1.58, 3.80)*	1.51 (0.90, 2.51)*
Distance of Treatment Location from Home was more than 0.5 km	0.97 (0.51-1.83)	1.48 (0.94-2.33)	1.39 (0.95-2.03)	0.95 (0.33-2.72)	0.001 (<0.001 to >999)	1.23 (0.55-2.75)	0.48 (0.18, 1.25)	0.17 (0.04, 0.76)	0.523 (0.21, 1.34)
Place of Treatment was Not Decided in Community Meeting involving kinship/neighborhood	0.90 (0.40-1.99)	1.242 (0.74-2.07)	1.29 (0.84-2.00)*	2.69 (0.77-9.36)	1.65 (0.56-4.81)*	0.91 (0.49-1.70)	3.84 (2.36, 6.22)*	2.21 (1.06, 4.63)*	0.554 (0.304, 1.01)
Distributors were Not Selected in a community meeting	0.81 (0.44-1.48)	1.85 (1.01-3.37)*	1.10 (0.72-1.67)*	1.78 (0.74-4.27)	1.43 (0.66-3.09)	0.58 (0.32, 1.03)	1.87 (1.04, 3.35)*	1.55 (0.95, 2.54)	1.25 (0.73, 2.13)
Did Not Give Anything to Distributors for Services	0.66 (0.25-1.79)	1.42 (0.64-3.61)	2.07 (1.33-3.22)*	1.32 (0.16-10.8)	1.49 (0.64-3.47)	1.02 (0.48 - 2.15)	0.40 (0.14, 1.19)	2.03 (1.19, 3.46)*	0.50 (0.23, 1.06)

^Odds ratios were calculated by comparing variables dichotomously with the reference levels remaining the same from Table 4
(i.e. Treatment location was not resident's house/compound was compared to treatment location being the residents' house/compound).
* Indicates significance at the 95% confidence level.