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Evaluation of Progress of Patients Exposed to Togo's National Lymphoedema Management Programme: A Longitudinal Study

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Evaluation of Progress of Patients Exposed to Togo's National Lymphoedema Management Programme: A Longitudinal Study

By

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2009

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Abstract

Evaluation of Progress of Patients Exposed to Togo's National Lymphoedema Management Programme: A Longitudinal Study

By Kira Harvey

Lymphatic Filariasis (LF), a mosquito-borne parasitic disease, can lead to permanent damage to the lymphatic system, causing lymphoedema. Patients experience bacterial infections, called acute adenolymphangitis attacks (ADLA), which can speed progression of disease. Lymphoedema management techniques have been shown to decrease incidence of ADLA, slowing progression of disease. In 2007, Togo's Ministry of Health and the Centers for Disease Control & Prevention started the National Lymphoedema Management Programme (NLMP). This program teaches lymphoedema patients lymphoedema management techniques in order to change treatment behavior and improve outcomes among patients. The purpose of this study is to use longitudinal data to evaluate the extent to which participation in the NLMP was associated with changes in treatment behavior, ADLA incidence, and quality of life. Data were collected annually from the same between 2007 and 2010. Paired analyses and longitudinal analyses were conducted in order to detect changes in responses over time.

Longitudinal analysis showed that use of promoted lymphoedema treatment methods increased significantly over time, and that patients whose symptoms had begun most recently (<10 years before 2007) experienced the greatest change in self-reported treatment behavior. Paired analyses found that use of many ineffective or harmful treatments also decreased significantly between 2007 and 2010. However, longitudinal analysis failed to detect a significant change in rate of ADLA over time. Paired analyses also failed to detect significant changes in most measures of quality of life.

Although patients participating in the NLMP in Togo experienced significant changes in self-reported lymphoedema management behaviors over time, this change was not accompanied by a reduction in ADLA incidence. There was also no evidence that self-sufficiency improved as a result of the program. However, it is not possible to know how outcomes would have been different in the absence of the NLMP. Studies using control groups and verification of self-report should be conducted in the future.

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Thank you to Dr. Mathieu for trusting me to analyze this dataset and for teaching me about the importance of neglected tropical disease management and control.

Thank you to Dr. Kleinbaum for teaching me about analysis of longitudinal data.

Contents

Chapter 1: Background and Literature Review

Lymphatic Filariasis Biology and Physical Effects

Lymphatic filariasis (LF), a mosquito-borne parasitic disease, is an important contributor to disability and morbidity in the developing world(1). This disease is caused by filariae worms, usually of the species *Wuchereria bancrofti,* which are transmitted via bites from infected mosquitoes. When an infected mosquito bites a person, it transfers microfilariae, the larval form of filariae worms, through the skin into the person's lymphatic system. After six months or longer, the microfilariae grow into adult filariae worms, mate, and deposit microfilariae into the lymphatic system. The microfilariae can migrate to the peripheral bloodstream. Without intervention, adult worms can live for up to seven years or longer and deposit millions of microfilariae. Mosquitoes that bite infected people can then transfer the microfilariae to new human hosts. Due to the inefficient lifecycle of the worms, humans typically must be exposed to repeatedly over a long period of time before they are infected (2).

Although infection is usually asymptomatic, the presence of adult worms can cause irreversible damage to lymphatic vessels, which can eventually lead to lymphoedema. Lymphoedema is caused by fluid collection in the lymph nodes, which results in swelling. Lymphoedema occurs most often in a leg, but it can also occur in the arms, breasts, or genitalia. When swelling occurs in the scrotum, it is called hydrocele(3). The severity of lymphoedema is classified into seven stages (detailed in table 1)(4). Without intervention, lymphoedema stage can progress over time.

Due to decreased functioning of the immune system that results from damage to the lymphatic system, lymphoedema patients may also experience recurrent secondary bacterial infections, known as acute adenolymphangitis attacks (ADLA), which are characterized by inflammation, swelling, and increased pain(2). Without intervention,

lymphoedema patients experience a mean annual incidence of between 1.6 and 7ADLA episodes that last between 1 and 16 days each(5). ADLA have been shown to contribute to the progression of lymphoedema stage. ADLA are also thought to lead to the hardening and thickening of the skin in the affected area, which is known as elephantiasis (6). The relationship between ADLA incidence rate and lymphoedema stage progression is supported by the fact that increased lymphoedema stage has been associated with increased rate of ADLA in some contexts (5). Taking measures to decrease rate of ADLA among patients may be able to slow the progression of lymphoedema, reducing morbidity and disability among infected individuals.

Lymphatic Filariaisis Psychosocial Effects

In addition to the aforementioned physical symptoms of LF, physical disability and social stigma can lead to negative psychological outcomes in affected individuals. According to a qualitative study, women with lymphoedema in both Ghana and the Dominican Republic face large amounts of stigma due to their lymphoedema. This stigma can lead to a variety of consequences, including social isolation, lack of access to employment, and reluctance to seek medical care (7). Social isolation is particularly problematic for lymphoedema patients due to the fact that, as symptoms progress, they may require assistance from others to complete routine tasks. Another qualitative study of Dominican female LF patients found that patient experience of psychological and social effects of lymphoedema that did not always correspond to the severity of physical symptoms (8). According to a study of lymphoedema patients compared to healthy family member controls in Sri Lanka, the physical limitations and social stigma associated with LF cause patients to have significantly lower physical, psychological, and overall quality of life scores than do healthy family members. This study also found that increased frequency of ADLA and increased lymphoedema stage were associated with decreased scores on some, but not all, quality of life measures(9). A study of lymphatic

filariasis patients found that over 70% were considered to be at high risk of depression (as defined by a score of >30 on the Duke Anxiety and Depression Scale), and that individuals with high risk of depression had higher lymphoedema stages and more days spent in ADLA per year in comparison with other patients(10).

Lymphatic Filaraisis Epidemiology

According to the World Health Organization (WHO), as of 2009, about 120 million people in 81 countries were infected with LF. Of these, about 40 million had clinical symptoms. This group of 40 million consisted of 25 million men with urogenital swelling, with hydrocele accounting for most cases, and 15 million people, the majority of whom were female, with lymphoedema (most often of the leg). In addition, about 1.34 million people were at risk of LF infection. Of these 1.34 million people, about 873 million (65%) lived in Southeast Asia and 406 million (30%) lived in Africa. The remaining 5% lived in other tropical areas (11). Because of the complex series of events that must occur from initial infection to the development of symptoms, most people who have repeat exposures to microfilariae in childhood do not develop clinical symptoms until after puberty (3). Although LF does not typically lead to death, the chronic physical limitations caused by lymphoedema caused the WHO to name it the second leading cause of chronic disability in the world in 1995 (12).

Global Programme to Eliminate Lymphatic Filariaisis

In 1997, the World Health Assembly resolved to eliminate LF as a public health problem (WHA Resolution 50.29). To meet the goal of eliminative LF, the WHO established the Global Programme to Eliminate Lymphatic Filariasis (GPELF). This program has two main goals –to interrupt transmission of LF infection and to alleviate suffering and disability among affected populations (13). Transmission can be thought to be interrupted after four to six years of annual administration of anti-parasitic drugs to

at risk communities (14). These anti-parasitic drugs kill the microfilaria, which are responsible for transmission of LF, and can even kill some of the adult worms. However, these drugs cannot reverse existing damage to the lymphatic system. In addition, many patients with chronic lymphoedema symptoms no longer have active infections with filariae worms. Therefore, therapy for patients with clinical symptoms must focus on basic management of symptoms and prevention of ADL attacks. Simple lymphoedema management treatments, including washing, elevation, and exercise, are recommended by the WHO for management of lymphoedema symptoms (15).

Although GPELF has been successful in working towards its goal of interrupting LF transmission, the morbidity management component has not received as much attention. At the time the 2009 progress report was published, only 27 (33%) of the LF-endemic countries had active morbidity management programs. This statistic includes countries that have programs that are only accessible to a portion of patients (e.g., one morbidity management clinic in the entire country). It also includes countries that offer hydrocele surgery or lymphoedema management, but not both. In its strategic plan for 2010-2020, the WHO plans to make it a priority for all LF-endemic countries to have active morbidity management programs by 2015. In order to evaluate whether this goal has been achieved, the WHO plans to begin collecting data on indicators related to morbidity management in 2014(11). Because countries are not currently required to report morbidity management activities to the WHO, it is unclear how many countries currently have comprehensive lymphoedema management programs.

Evidence for the Effectiveness of Lymphoedema Morbidity Management

The principle behind the WHO-recommended lymphoedema morbidity management measures is that simple, inexpensive measures, including elevation, exercise, and washing of the affected limb, will decrease the incidence of ADLA. This decreased ADLA incidence will then slow progression of lymphoedema and reduce the

morbidity and disruption to productivity caused by the disease. An advantage of this lymphoedema management paradigm is that it requires very few resources. Once patients are trained and given basic start-up supplies, they do not require assistance from health-care personnel to manage their lymphoedema.

Studies have demonstrated that basic lymphoedema management techniques are successful in reducing ADLA incidence. Patients enrolled in a randomized trial of anti-bacterial soap versus plain soap in Leogane, Haiti experienced a decrease in ADLA from 1.1 per person-year before the intervention to 0.40 per person-year after the intervention (whether the soap was anti-bacterial or plain did not have any impact on ADL attack incidence) (16). In Leogone, Haiti, when the lymphoedema management clinic switched its primary method of management from bandaging (a previously-used method that has been shown to be harmful) to basic hygiene measures, ADL attack incidence decreased from 1.56 per person-year to 0.48 per person-year (17). This change reflects the combined effect of effective treatment and the removal of a harmful practice.

Studies have also demonstrated that simply training patients in home-based management for lymphoedema and providing start-up materials (e.g. soap and towels) can lead to significant reductions in ADLA incidence rates. According to a WHO study, introduction of a home-based lymphoedema management program for patients in Sri Lanka, Zanzibar, and Madagascar was associated with a dramatic decrease in ADLA and LF clinic visits in all three countries. Significant decreases of ADLA rates occurred in patients in all three countries, despite the fact that patients in Sri Lanka had monthly clinic visits, whereas patients in Zanzibar and Madagascar did not(11). In Burkina Faso, a lymphoedema self-care program reduced percent of patients who reported an ADLA in the month before consultation from almost 80% to less than 40% (18). The results of these studies suggest that, when patients are trained to treat their own lymphoedema at home, substantial decreases in ADLA rate can occur.

Although the association between lymphoedema management and decreased ADLA rate is well-documented, relatively few studies regarding the effect of morbidity management on psychosocial outcomes among patients have been published. One study about patients in Guyana found that patients' scores on the Dermatology Quality of Life Scale improved significantly after participation in a morbidity management program (19). The Dermatology Quality of Life Scale contains a series of questions related to the extent to which skin problems affect an individual's psychosocial well-being and activity participation(20). However, in order to appropriately assess the extent to which lymphoedema management programs impact quality of life for lymphoedema patients, it is important for a disease-specific lymphoedema quality of life index to be designed (21).

Lymphatic Filariaisis in Togo

In Togo, a country in West Africa with a population of 6.1 million, 7 of the 35 health districts in the country, encompassing 1.19 million people (22), were endemic for LF in 2007 (23). Citizens of LF-endemic districts in Togo received annual mass drug administration (MDA) to prevent LF beginning between 2000 and 2002. In 2009, LF transmission in Togo was considered to be interrupted, and all MDA was ceased. However, because damage to the lymphatic caused by LF is often irreversible, there remains a population in need of lymphoedema management.

Togo's National Lymphoedema Management Programme

With technical assistance from the Centers for Disease Control & Prevention and funding from the IMA Worldhealth and the United States Agency for International Development, Togo's Ministry of Health established the National Lymphoedema Management Programme (NLMP) in 2007. This program was designed to provide a low-cost model that can be maintained without sustained financial support and replicated in other low-resource, LF-endemic countries. The NLMP employs three main strategies –

train at least one staff member in each health facility about basic lymphoedema management, make patients aware that dispensaries can teach them about morbidity management, and train patients to use washing, elevation, and exercise to care for their own swollen limbs.

In order to train the health staff, the CDC and the Togo Ministry of Health published a training manual that details lymphoedema self-care techniques in words and pictures. This manual was utilized in all trainings. The national program coordinator trained district health staff, who in turn trained local hospital directors. Local hospital directors trained nurses, who then trained village health volunteers. Staff at all local hospitals were then equipped to train lymphoedema patients in basic lymphoedema management techniques

In order to disseminate the message that lymphoedema treatment is available to affected individuals, messages that people with swollen limbs should go to the dispensary were disseminated through the healthcare structure, the political structure, and through general advertising methods (e.g. posters, TV, and radio). Patients who came to the local dispensary for training were trained in lymphoedema management by the hospital directors. Patients who came for training were provided with soap and clean towels. This one-time gift of materials was given to patients with the understanding that patients would purchase their own materials in the future. Patients in endemic districts then had follow-up visits with community health volunteers (initially weekly, then every other week, and then monthly) in order to ensure that they were continuing to practice appropriate lymphoedema management techniques.

The Purpose of this Study

The NLMP was designed to be a low-cost, sustainable protocol for promoting appropriate lymphoedema management in patients with chronic lymphoedema symptoms. If this program is effective at promoting appropriate lymphoedema

management in patients and improving physical, psychological, and social outcomes for patients, it will be replicated in other low-resource settings that are endemic for LF. Although current research solidly supports the claim that basic lymphoedema management techniques can reduce incidence of ADLA, very little published data has examined the impact of lymphoedema management on the psychological or social outcomes of patients over time. Longitudinal analyses will be conducted to examine the relationship between year (a proxy for years of exposure to the NLMP) and two outcome variables –proportion of respondents reporting current use of at least one promoted treatment and number of ADLA in the past year. Paired analyses will also examine the use of non-promoted treatments and quality of life of the patients in 2010 compared to 2007. The results of this study will identify strengths of the program and provide areas for program improvement.

Chapter 2: Manuscript

Introduction

Lymphatic filariasis (LF), a mosquito-borne parasitic disease, is an important contributor to disability and morbidity in the developing world (1). This disease is caused by filariae worms, usually of the species *Wuchereria bancrofti*, which are transmitted via infected mosquitoes. Although infection is usually asymptomatic, the presence of adult worms can cause irreversible damage to lymphatic vessels, which can lead to lymphoedema and hydrocele. People with LF may also experience recurrent secondary bacterial infections, known as adenolymphangitis attacks (ADLA), which are characterized by inflammation, swelling, and increased pain (3). Without intervention, lymphoedema patients experience a mean annual incidence of between 1.6 and 7ADLA episodes that last between 1 and 16 days each (5). ADLA have also been shown to contribute to the progression of lymphoedema stage (for a description of lymphoedema stages, see table 1). ADLA are also thought to lead to the hardening and thickening of the skin in the affected area, which is known as elephantiasis (4).

In addition to the aforementioned physical symptoms of LF, physical disability and social stigma can lead to negative psychological outcomes in affected individuals. It is common for LF patients to report feeling depressed, embarrassed (8), isolated, and stigmatized (7) due to the condition. Because of the physical limitations and social stigma associated with LF, patients have significantly lower physical, psychological, and overall quality of live scores than do healthy family members (9).

In 1997, the World Health Assembly resolved to eliminate LF as a public health problem (WHA Resolution 50.29). To meet this goal, the World Health Organization (WHO) established the Global Programme to Eliminate Lymphatic Filariasis (GPELF). This program has two main goals –to interrupt transmission of LF infection and to

alleviate suffering and disability among affected populations (13). Transmission can be interrupted through annual administration of anti-parasitic drugs to at risk communities. These anti-parasitic drugs kill the microfilaria, which are responsible for transmission of LF, and can even kill the adult worms, which are responsible for the onset of lymphoedema symptoms. However, these drugs cannot reverse existing damage to the lymphatic system. Therefore, therapy for affected individuals must focus on basic management of symptoms and prevention of ADLA. Simple lymphoedema management treatments, including washing, leg elevation, and leg rotation, are recommended by the WHO for LF symptom management (15).

Although GPELF has been successful in working towards its goal of interrupting LF transmission, the morbidity management component has not received as much attention. At the time the WHO's 2009 progress report was published, only 27 (33%) of the LF-endemic countries had active morbidity management programs. This statistic includes countries that have programs that are only accessible to a portion of patients, as well as countries that offer hydrocele surgery or lymphoedema management, but not both (11). Because countries are not currently required to report morbidity management activities to the WHO, it is unclear how many countries currently have comprehensive lymphoedema management programs.

In Togo, a country in West Africa with a population of 6.1 million, 7 of the 35 health districts in the country, encompassing 1.19 million people (22), were endemic for LF in 2007 (23). Citizens of LF-endemic districts in Togo received annual mass drug administration (MDA) to prevent LF between 2000 and 2009. In 2009, LF transmission in Togo was considered to be interrupted, and all MDA was ceased.

With technical assistance from the Centers for Disease Control & Prevention and financial assistance from the United States Agency for International Development and IMA Worldhealth, Togo's Ministry of Health established the National Lymphoedema

Management Programme (NLMP) in 2007. This program was designed to provide a low-cost model that can be maintained without sustained financial support and replicated in other low-resource, LF-endemic countries. The NLMP employs three main strategies – train at least one staff member in each health facility about basic lymphoedema management, make patients aware that dispensaries can teach them about morbidity management, and train patients to care for their own swollen limbs. The main morbidity management methods promoted by the NLMP include WHO-recommended strategies such as washing, elevation, and exercise of the affected limb.

Although current research solidly supports the claim that basic lymphoedema management techniques can reduce incidence of ADLA, very little published data has examined the impact of lymphoedema management on the psychological or social outcomes of patients over time. With the goal of assessing the effects of the NLMP on treatment practices, lymphoedema symptoms, ADLA incidence, psychological well-being, and quality of life of LF patients, we conducted a longitudinal study of a cohort of LF patients throughout Togo. The purpose of this paper is to use the data gathered by these surveys to evaluate the impact of the NLMP on LF patients in Togo.

Methods

Data Collection Methods

An in-person survey was conducted in six of the seven LF-endemic districts of Togo in June and July every year from 2007 until 2010. The survey cohort was a convenience sample, and the same individuals were surveyed each year. The interviews were conducted by three pairs of interviewers. Each pair consisted of one person trained specifically to use a personal digital assistant (PDA) and administer the questionnaire and one person who was medically trained and fluent in the local language. The questionnaire included a structured set of questions and pre-defined responses, and it

was translated verbally from French into local languages (for more details regarding data collection methods, see Richard et al. (10)).

Survey Questions

The questions asked in the survey that will be addressed in this analysis fall into the following categories –demographic information, medical history, lymphoedema symptoms and treatment, ADLA symptoms and treatment, and quality of life. Interviewers also took photographs of the patients' legs and asked questions about economic issues, but these aspects will not be addressed here. Demographic information obtained included age, sex, occupation, ethnicity, and district. Medical history obtained included years of lymphoedema symptoms and years of severe lymphoedema symptoms prior to 2007. Lymphoedema symptom and treatment questions were asked in order to determine the patient's lymphoedema stage and the patient's use of promoted and non-promoted lymphoedema treatments. ADLA symptom and treatment questions were asked in order to ascertain the frequency and duration of ADLA, as well as the patients' responses to these attacks. Quality of life questions were asked in order to ascertain the degree to which the patient's symptoms affected her daily activities, the amount of help that the patient needed and obtained from others, the amount of social stigma the patient faced, and the patient's score on the Duke Anxiety-Depression (DUKE-AD) scale (for more information about the DUKE-AD scale, see Parkerson et al (24)).

Data Analysis

All analyses were performed using SAS Version 9.2 (SAS Institute Inc., Cary, NC, USA). To compare demographic composition and initial symptom severity between all patients surveyed in 2007, patients who were surveyed in 2007 and 2010, and patients who were surveyed all four years, one-sample sign-rank tests were used for continuous variables and chi-square analyses were used for nominal variables. Descriptive statistics for individual survey questions included frequencies and percentages by year for yes-no

questions and means, standard deviations, medians, minimums, and maximums for continuous and ordinal questions. To compare paired responses between 2007 and 2010, McNemar's tests were used for yes-no questions and sign-rank tests were used for continuous and ordinal questions. For yes-no questions, Mantel-Haenszel odds ratios (mOR's) were also calculated. Confidence limits of the mOR's were calculated using the mid-p exact method (25). This method was used because some of the comparisons had few (<20) discordant pairs. All questions that had the answer choices "a lot," "a little," and "none" were converted to yes-no questions for paired analyses. Answers of "a lot" were considered to be of "yes," and "a little" and "none" were considered to be "no".

Longitudinal Analysis

In order to further examine the change in patients' behavior, symptoms, and psychological well-being over time while controlling for potential confounding and interaction, two multivariate longitudinal models were analyzed. First, generalized estimating equation (GEE) analysis of a correlated logistic regression model was used to model the proportion of the patients that reported use of at least one of the promoted treatments. Next, generalized estimating equation (GEE) analysis of a correlated Poisson regression model was used to model the number of ADLA in the past year.

For both models, the main predictor of interest was year. The linearity of the association between each outcome variable and year was assessed graphically. If the graphical association over time visually appeared to be linear, year was added to the model as one ordinal variable with the levels 0 to 3 to denote number of years of exposure to the NLMP (patients in 2007 had 0 years of exposure). If the association was not linear, year was added to the model as three dummy variables with 2007 as the reference year. The first year of observation (2007) was used as the reference year because it represents the conditions before the implementation of the NLMP, and the

main research objective is to assess the impact of participation in the NLMP on patient outcomes.

Potential confounders considered for the models included age (a categorical variable defined as follows: under 35, 35-60, and over 60), years since lymphoedema symptoms began (a categorical variable defined as follows: under 10 years, 10-30 years, and over 30 years), years since lymphoedema symptoms became severe (a categorical variable defined as follows: under 10, 10-20, and over 20 years), and district (defined as follows: Kozah, Tone, and other). All age and disease history variables refer to 2007 levels. The interactions of each of the aforementioned confounders and year were also considered for the models. For both outcomes, all potential confounders and interaction terms were initially included in the initial multivariate model. The model was then tested for collinearity. In the case of a collinarity problems, as indicated by a condition index (CI) of greater than 30, interaction terms involved in the collinearity problems (i.e. terms with VDP above 0.5) were removed from the model one at a time until the CI is below 30. After this, backwards elimination was used to remove interaction terms that were not associated with the outcome at the $p=0.10$ level. Next, backwards elimination was used to remove all potential confounders that were not involved in remaining interaction terms, did not change the association between year and outcome by more than 10%, and whose removal led to an increase in precision (defined as a narrowing of the 95% confidence interval). The remaining interaction terms and confounders were included in the final multivariate model.

Because these are longitudinal models, the model selection process was conducted assuming a stationary (3-dependent) correlation structure. In order to decide whether stationary was the appropriate correlation structure for each model, the final multivariate model was examined in each of four correlation structures –stationary (3-dependent), autoregressive (1), exchangeable, and unstructured. For each correlation

structure, QIC and difference between model-based and empirical standard errors were noted. If a correlation structure other than stationary had a substantially lower QIC and lower differences between model-based and empirical standard errors, this structure was used for analysis. If the results of these tests were unclear, a stationary correlation structure was used for analysis. In order to account for the fact that the chosen correlation structure is not the correct correlation structure for the data, empirical estimates of standard error were used for analysis of both models.

Ethics

This study was classified as non-human subjects research by the Emory University Institutional Review Board (IRB). Therefore, it did not require IRB approval (see appendix 2).

Results

Demographic Characteristics

In 2007, 166 patients were interviewed. However, not all of these patients were surveyed all four years. The frequency tables will only include patients that were surveyed all four years (n=93). For the paired tests, only the patients that were surveyed in both 2007 and 2010 were included (n=107). We will include in the longitudinal models all patients who were surveyed in both 2007 and at least one of the other three years (n=150).

Of the 150 patients surveyed in 2007 and at least one other year, the median age was 48 (range:6-90) and 57% were female. Most of the patients lived in the districts Tone (35%) and Kozah (25%) and were members of the ethnolinguistic groups Kabye (37%) and Moba (25%). In 2007, the patients had been suffering from LF symptoms for a median of 18 years (range:4-63), had been suffering severe LF symptoms for a median of 12 years (range:4-58), had a median LF stage of 3 (range:0-6), and reported a median of 2 (range:0-18) ADLA in the past year. The patients who were lost to follow-up after

2007 have demographic characteristics and initial LF symptoms that are not different from the full cohort (see table 2).

Frequencies

Frequency tables including only individuals surveyed all four years (n=93) were created. The number and percentage of respondents who answered yes to each yes-no question by year is provided in table 3. The mean, standard deviation, median, minimum, and maximum for each interval and ordinal question by year is provided in table 4.

Percent of respondents who reported that they currently use each of the lymphoedema treatments promoted by the NLMP (elevation, exercise, and washing) increased substantially over the four years (19.4% to 80.0%, 4.3% to 81.7%, and 8.6% to 94.6%, respectively). Percent of respondents reporting current use of at least one promoted treatment also increased substantially over the four years (24.7% to 97.9%). However, the percent of patients whose affected legs appeared to be visually clean fluctuated among years.

Over the same time period, percent of respondents who reported current use of lymphoedema treatments not promoted by NLMP (herb application, herb consumption, hot compresses, scarification, and no treatment) decreased substantially (16.1% to 1.1%, 10.8% to 0%, 6.5% to 1.1%, 7.5% to 1.1%, and 33.3% to 2.2%, respectively). Practically no patients in any year (1 in 2009, none in the other years) reported use of compression. Percent of respondents who reported current use of some ADLA treatments not promoted by NLMP (traditional product application, herb consumption, and scarification) also decreased substantially (20.4% to 4.3%, 11.8% to 1.1%, and 6.5% to 0%, respectively). However, percent of respondents who reported current use of other ADLA treatments, including compresses, ointment, prayers, and no treatment, did not show an increasing or decreasing trend over time.

None of the other categorical variables showed clear upward or downward trends over time. However, the percent of patients reporting that friends/neighbors and community members offered them "a lot" of help in the past week decreased substantially after the first year (20.4% in 2007 to 4.3% in 2008 and 17.2% in 2007 to 3.2% in 2008, respectively) and then leveled off.

The only ordinal or interval variable that showed a clear trend over time was duration of ADLA. The duration of ADLA decreased from a mean of 6.27 days (std=4.76) and a median of 6 days in 2007 to a mean of 4.59 days (std=2.92) and a median of 4 days in 2010. However, the number of ADLA per year did not appear to increase or decrease over time.

Paired analyses

Paired analyses between responses from the first and last years of the study were conducted on data from all patients that were surveyed in both 2007 and 2010 (n=107). For each question, only responses for individuals who responded to that particular question in both 2007 and 2010 were included in analysis. For all yes-no survey questions, McNemar's paired analyses were used (see table 5). For all interval and ordinal survey questions, paired sign-rank tests were used (see table 6).

Lymphoedema stage ($p=0.64$) and number of ADLA per year ($p=0.15$) did not change significantly between 2007 and 2010. Duration of ADLA decreased significantly from a median of 6 (range 1-21) days in 2007 to 4 (range 1-15) days in 2010 ($p=0.05$). However, number of days that ADLA caused respondents to miss work ($p=0.63$) did not change significantly.

The proportion of patients reporting use of promoted lymphoedema treatments increased significantly from 2007 to 2010. Proportion of respondents reporting elevating their affected leg increased from 18% to 77% ($p<0.0001$). Proportion of respondents reporting exercising their affected leg increased from 4% to 79% ($p<0.0001$). Proportion

of respondents reporting washing their leg increased from 10% to 93% ($p<0.0001$). Proportion of respondents reporting use of at least one of the aforementioned treatments increased from 25% to 95% ($p<0.0001$). These responses are corroborated by the fact that the proportion of respondents whose affected leg appeared to be clean increased from 45% to 65% ($p=0.0002$).

The proportion of patients who reported use of ineffective or harmful lymphoedema treatments decreased between 2007 and 2010. Proportion of patients reporting applying herbs to their legs decreased from 22% to 2% ($p<0.0001$). In 2007, 12% of respondents reported drinking herbs to treat lymphoedema. In 2010, no patients reported this. Proportion of patients reporting using hot compresses ($p=0.025$), scarification ($p=0.020$), and using no treatment at all ($p<0.0001$) also decreased between 2007 and 2010.

The proportion of patients who reported use of some ineffective or harmful ALDA treatments also decreased. Proportion of patients reporting applying traditional products to treat ADLA decreased from 24% in 2007 to 5% in 2010 ($p<0.0001$). Proportion of patients reporting drinking herbs ($p=0.0013$), applying a hot compress ($p=0.014$), and applying ointment ($p=0.029$) also decreased significantly between 2007 and 2010. Proportion of patients reporting praying ($p=0.10$) or doing nothing ($p=0.41$) did not decrease significantly between 2007 and 2010. However, few patients (<10%) reported using these treatments in either year.

The proportion of patients who reported that their lymphoedema symptoms prevented them from washing ($p=0.0047$) or getting out of bed ($p=0.0047$) increased significantly between 2007 and 2010. However, the percentage of patients who reported these difficulties in 2010 remained low (7.4%). Proportion of patients reporting difficultly working in the field ($p=0.71$), going to market ($p=0.81$), sweeping ($p=0.096$),

fetching water (p=0.21), going to the courtyard (p=0.16), or carrying heavy burdens (p=0.86) did not change significantly over time.

The proportion of patients who reported that they required a lot of (as opposed to a little or no) help from family members in their households (p=0.79), family members who did not live with them (p=0.52), friends or neighbors (p=0.53), or community members (p=0.33) did not change between 2007 and 2010. The proportion of respondents who reported that family members living with them (p=0.14) or family members living elsewhere (p=0.42) offered them a lot of help (as opposed to little or no help) in the past week also did not change between 2007 and 2010. However, the proportion of respondents who reported that friends or neighbors offered them a lot of help in the past week decreased from 20% to 4% (p=0.0007), and the proportion of respondents who reported that other community members offered them a lot of help in the past week decreased from 16% to 3% (p=0.0017). The proportion of patients who reported feeling shunned by family members living with them (p=1), family members not living with them (p=0.71), friends or neighbors (p=0.78), or other community members (p=0.47) also did not change between 2007 and 2010.

Longitudinal Analysis

A GEE analysis of a correlated logistic regression model was used to model the effect of year on proportion of respondents who reported use of at least one promoted lymphoedema treatment. The relationship between year and the log-odds of reporting use of at least one promoted lymphoedema treatment was linear (see figure 1). Therefore, for this analysis, year was coded as an ordinal variable with values 0-3 representing years since initial program implementation. There were no collinearity problems in the initial multivariate model (CI=18.11). Therefore, all potential confounders and interaction terms were included in the initial multivariate model. The only potential interaction effect that was significant was the product of the “year”

variable with the variable “years since symptoms began” (coded in three categories –less than 10 years, 10-30 years, greater than 30 years). No potential confounders changed the odds ratio (OR) relating exposure to outcome by 10% or more. However, the removal of sex from the model led to a decrease in precision. Therefore, sex was included in the final multivariate model (see table 6). Of the four correlation structures considered for this model, stationary (3-dependent) had the lowest QIC goodness of fit criterion. The unstructured correlation structure had the lowest difference between model-based and empirical standard errors (see table 7). Because it is more plausible for longitudinal data to follow a stationary correlation structure than an unstructured correlation structure, a correlation structure of stationary (3-dependent) was used for the final model.

A total of 467 observations from 137 individuals were included in this analysis. Of these individuals, 29 had symptoms that began less than 10 years ago, 83 had symptoms that began between 10 and 30 years ago, and 25 had symptoms that began more than 30 years ago. For patients whose symptoms began less than 10 years ago, the odds of reporting use of at least one promoted treatment increased by almost nine times between 2007 and 2008 (OR=8.83, 95% CI: 3.86, 20.20), almost eighty times between 2007 and 2009 (OR=78.04, 95% CI: 14.93, 407.93), and by over 600 times between 2007 and 2010 (OR=689.39, 95% CI: 57.69, 8239.72). For patients whose symptoms began between 10 and 30 years ago, the odds of reporting use of at least one promoted treatment increased by almost three times between 2007 and 2008 (OR=2.93, 95% CI: 2.15, 4.01), over eight and a half times between 2007 and 2009 (OR=8.61, 95% CI: 4.61, 16.05), and twenty-five and a quarter times between 2007 and 2010 (OR=25.25, 95% CI: 9.91, 64.32). For patients whose symptoms began more than 30 years ago, odds of reporting use of at least one promoted treatment increased by over two and four-fifths between 2007 and 2008 (OR=2.81, 95% CI: 1.78, 4.44), almost eight times between

2007 and 2009 (OR=7.92, 95% CI: 3.18, 19.74), and over twenty-two and a quarter times between 2007 and 2010 (OR=22.29, 95% CI: 5.67, 87.74) (see table 8).

A GEE analysis of a correlated Poisson regression model was used to model the effect of year on number of ADLA per year. The relationship between year and the log-rate of ADLA per year was not linear (see figure 2). Therefore, for this analysis, year was coded as three dummy variables with 2007 as the reference year. The initial multivariate model had collinearity problems (CI=54.335). In order to rectify this problem, interaction between year and district and interaction between year and years since symptoms became severe were removed from analysis; note that because these variables was removed because of collinearity, we were unable to assess their significance . After these interaction terms were removed, there was no longer a collinearity problem (CI=21.24).. The only potential interaction effect that was significant was years since symptoms began (coded in three categories –less than 10 years, 10-30 years, greater than 30 years). No potential confounders changed the incidence rate ratio (IRR) relating exposure to outcome by 10% or more. Removal of each confounder resulted in improvement of precision (see table 9). Therefore, no terms other than year, years since symptoms began, and the interaction between year and years since symptoms began were included in the final model. Of the four correlation structures considered for this model, unstructured had the lowest QIC goodness of fit criterion and the lowest difference between model-based and empirical standard errors (see table 10). Although it is more plausible for longitudinal data to follow a stationary or autoregressive (1) correlation structure than an unstructured correlation structure, the results of these tests suggest that unstructured is the appropriate correlation structure for this model. Therefore, an unstructured correlation structure was used for the final multivariate model.

A total of 348 observations from 134 individuals were included in this analysis. Of these individuals, 29 had symptoms that began less than 10 years ago, 81 had symptoms that began between 10 and 30 years ago, and 24 had symptoms that began more than 30 years ago. For patients whose symptoms began less than 10 years ago, the rate of ADLA increased by about two and two-fifths times between 2007 and 2008 (IRR=2.41, 95% CI: 1.37, 4.26). However, the rate of ADLA was not significantly higher in 2009 (IRR=1.15, 95% CI: 0.82, 1.63) or 2010 (IRR=1.18,95% CI: 0.81, 1.71) than in 2007. For patients whose symptoms began between 10 and 30 years ago, rate of ADLA was not significantly different from rate in 2007 either 2008 (IRR=1.44, 95% CI: 0.90, 2.31) or 2010 (IRR=1.06, 95% CI: 0.83, 1.35). However, in comparison with 2007, ADLA rate in 2009 was twice as high for patients whose symptoms began between 10 and 30 years ago (IRR=2.01, 95% CI: 1.46, 2.75). For patients whose symptoms began more than 30 years ago, ADLA rate did not change significantly from 2007 to 2008 (IRR-1.44, 95% CI: 0.95, 2.16), 2007 to 2009 (IRR: 0.86, 95% CI:0.59, 1.24), or 2007 to 2010 (IRR=1.27, 95% CI: 0.76, 1.13) (see table 11).

Discussion

The purpose of this study was to use longitudinal data to evaluate the extent to which exposure to the NLMP was associated with changes in treatment behaviors, lymphoedema symptoms, ADLA frequency and severity, and quality of life among Togolese lymphoedema patients. Because all subjects were exposed to the treatment beginning in 2007, year was used as a proxy for number of years in the treatment program. The results of both paired analyses and longitudinal analyses strongly suggest that 1-3 years of exposure to the NLMP was associated with an increase in promoted lymphoedema treatment practices among patients in comparison with pre-program conditions. The effect was particularly strong for patients whose symptoms began less than 10 years before 2007. This implies that future efforts of the NLMP and any

replication programs should add additional focus on reaching patients who have been suffering from lymphoedema for ten or more years. Paired analyses also suggest that a decrease in non-promoted lymphoedema treatment practices (including ineffective and potentially harmful treatments) occurred after exposure to the NLMP. These results all support the claim that the NLMP was effective at changing patient treatment behaviors.

However, the ultimate goal of improving patient treatment behaviors was to improve patient outcomes. This study did not demonstrate that patient outcomes improved significantly over time. Longitudinal analysis did not show that rate of ADLA decreased significantly over time in patients, regardless of the length of time since the patient's symptoms began. This null result conflicts with published studies regarding the effect of lymphoedema management on ADLA rate. It is unclear why ADLA rate failed to decrease as proportion of patients utilizing lymphoedema management techiniques increased. This could be because patients reporting using lymphoedema management techniques when they did not use them or used them improperly. Contrarily, it is possible that ADLA rate decreased and patients misremembered the number of ADLA that they had experienced in the past year. This could also be due to the low initial rate of ADLA in the study population.

The results of paired analyses do not support the claim that participation in the NLMP leads to increased self-sufficiency. Patients did not experience significant gains in any measures of self-sufficiency (reported need for help or effect of symptoms on daily activities) between 2007 and 2010. It is possible that, in the absence of the program, patients would have deteriorated. If this were the case, the lack of significant changes in most measures of self-sufficiency would be seen as a positive outcome. However, given the lack of a control group in this study, it is unclear whether self-sufficiency patients would have deteriorated over the four-year period in the absence of the program.

A secondary goal of the NLMP was to decrease social stigma of patients through open discussion of lymphoedema. There is no evidence that progress towards this goal was made during the first few years of the program. Proportion of patients reporting feeling shunned by family members, neighbors, and community members did not change significantly over time. In addition, in 2010, a decreased proportion of patients reported feeling as though friends/neighbors and community members offered them substantial amounts of help, in comparison with 2007. This decrease occurred even as the proportion of patients who reported needing a lot of help did not change significantly. These results suggest that, in the future, NLMP should invest more in decreasing stigma surrounding lymphoedema.

However, according to paired analysis, the DUKE-AD scores of patients decreased significantly between 2007 and 2010. It is unclear why this improvement occurred even though program participation was not associated with significant improvements in ADLA rate, self-sufficiency, or stigma. It is possible that increased attention from healthcare personnel or hope that lymphoedema management treatments would improve their symptoms improved patients' psychological well-being. It is also possible that psychological well-being would have improved over time even if the program had not been established.

Because these data were based entirely on self-report, it is possible that they are unreliable. In order to determine how reliable self-report is in this context, future studies should be conducted using methods to verify information obtained through self-report. In addition, it is difficult to make generalizations about the impact of a program without a comparison group. Therefore, future studies should compare individuals exposed to a lymphoedema management program to individuals who were not exposed. In order to properly assess the effect of national lymphoedema management programs on the treatment practices, lymphoedema symptoms, ADLA, and quality of life of lymphoedema

patients, more data is necessary. Specifically, studies involving a comparison population and a data source other than self-report may lead to more clear results.

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Tables

Lymphoedema Stage	Symptoms
Stage 1	Swelling is reversible overnight
Stage 2	Swelling is not reversible overnight
Stage 3	Shallow skin folds
Stage 4	Knobs
Stage 5	Deep skin folds
Stage 6	Mossy lesions
Stage 7	Unable to care for self or perform daily activities

Table 1: Lymphoedema stage classification

	Comparisons between Total Sample and Subsamples							
	Surveyed in 2007 (n=166)		Surveyed in 2007+1 other year (n=150)			Surveyed all 4 years (n=93)		
Characteristic	n	Median (Min-Max)	n	Median (Min-Max)	p	n	Median (Min-Max)	P
Age in 2007	143	48 (6-90)	136	48 (6-90)	1	88	47.5 (6-80)	0.91
Years since onset of LF symptoms (as of 2007)	144	18 (4-63)	137	18 (4-63)	1	87	18 (4-58)	1
Years since LF symptoms became bad (as of 2007)	136	12 (4-58)	130	12 (4-58)	1	83	11 (4-53)	0.82
Lymphoedema stage in 2007	164	3 (0-6)	150	3 (0-6)	0.19	93	3 (0-6)	0.2
Number of ADLA in 2007	163	2 (0-18)	147	2 (0-18)	0.22	93	2 (0-18)	0.28
	# (%)		# (%)		p	# (%)		P
Female	89 (53.61%)		85 (57%)		0.55	54 (58%)		0.50

Table 2: Demographic and initial symptoms information

Variable	2007 YES % (n)	2008 YES % (n)	2009 YES % (n)	2010 YES % (n)
Currently Using Effective Lymphoedema Treatments				
Elevation of the foot	19.4% (18)	46.2% (43)	76.3% (71)	80.0% (74)
Exercises	4.3% (4)	47.3% (44)	69.9% (65)	81.7% (76)
Washing	8.6% (8)	64.5% (60)	80.7% (75)	94.6% (88)
Elevation, exercise, and/or washing	24.7% (23)	65.6% (61)	81.7% (76)	97.9% (91)
Leg is clean	40.9% (38)	76.3% (71)	78.5% (73)	63.4% (59)
Currently Using Ineffective/Harmful Lymphoedema Treatments				
Applying herbs	16.1% (15)	7.5% (7)	5.4% (5)	1.1% (1)
Drinking herbs	10.8% (10)	1.1% (1)	1.1% (1)	0% (0)
Hot compress	6.5% (6)	1.1% (1)	2.2% (2)	1.1% (1)
Scarification	7.5% (7)	0% (0)	0% (0)	1.1% (1)
Compression	0% (0)	0% (0)	1.1% (1)	0% (0)
Nothing	33.3% (31)	12.9% (12)	4.3% (4)	2.2% (2)
Currently using ADLA Treatments				
Applying traditional	20.4% (19)	3.2% (3)	5.4% (5)	4.3% (4)

products				
Drinking herbs	11.8% (11)	1.1% (1)	1.1% (1)	1.1% (1)
Compress	6.5% (6)	2.2% (2)	0% (0)	1.1% (1)
Ointment	11.8% (11)	3.2% (3)	5.4% (5)	7.5% (7)
Prayers	4.3% (4)	0% (0)	4.3% (4)	1.1% (1)
Scarification	6.5% (6)	1.1% (1)	0% (0)	0% (0)
Nothing	9.7% (9)	3.2% (3)	14.0% (13)	6.5% (6)
Activities that Lymphoedema Symptoms Prevent Patient from Performing				
Working in the field	20.4% (19)	24.7% (23)	26.9% (25)	22.6% (21)
Going to the market	18.3% (17)	26.9% (25)	26.9% (25)	17.2% (16)
Sweeping	4.3% (4)	7.5% (7)	8.6% (8)	7.5% (7)
Washing	0% (0)	4.3% (4)	5.4% (5)	7.5% (7)
Getting out of bed	0% (0)	5.4% (5)	6.5% (6)	7.5% (7)
Fetching Water	7.5% (7)	14.0% (13)	9.7% (9)	17.2% (16)
Going to the courtyard	2.2% (2)	6.5% (6)	7.5% (7)	5.4% (5)
Carrying Heavy Burdens	23.7% (22)	35.5% (33)	40.9% (38)	32.3% (30)
People from whom Patients have needed help in the past week*				
Family members living with them	46.2% (43)	43.0% (40)	58.0% (54)	39.8% (37)
Family members not living with them	24.7% (23)	30.1% (28)	37.6% (35)	24.7% (23)
Friends/Neighbors	19.4% (18)	22.6% (21)	28.0% (26)	20.4% (19)
Community Members	17.2% (16)	20.4% (19)	32.3% (30)	19.4% (18)
People who have offered the patient help in the past week*				
Family members living with them	53.8% (50)	39.8% (37)	53.8% (50)	37.6% (35)
Family members not living with them	28.0% (26)	14.0% (13)	14.0% (13)	16.1% (15)
Friends/Neighbors	20.4% (19)	4.3% (4)	6.5% (6)	3.2% (3)
Community Members	17.2% (16)	3.2% (3)	5.4% (5)	2.2% (2)
People who have avoided the patient in the past week				
Family members living with them (EVF)	1.1% (1)	4.3% (4)	3.2% (3)	1.1% (1)
Family members not living with them (EVFN)	1.1% (1)	4.3% (4)	4.3% (4)	4.3% (4)
Friends/Neighbors (EVA)	5.4% (5)	10.8% (10)	8.6% (8)	7.5% (7)
Community Members (EVC)	7.5% (7)	10.8% (10)	7.5% (7)	6.5% (6)

*yes=”a lot,” no=”none” or “a little”

Table 3: Frequency table for responses to yes-no questions among patients surveyed all 4 years

Variable	2007			2008			2009			2010		
	N	Mean (std)	Med (min-max)	n	Mean (std)	Med (min-max)	n	Mean (std)	Med (min-max)	N	Mean (std)	Med (min-max)
Lymphoedema Stage	93	3.1 (1.6)	3 (0-6)	93	3.0 (2.1)	3 (0-6)	93	3.0 (1.7)	2 (0-6)	93	3.1 (1.9)	3 (0-6)
Number of ADLA per year	93	2.04 (2.3)	2 (0-18)	93	1.8 (4.2)	1 (0-36)	93	2.0 (2.8)	2 (0-15)	93	1.6 (1.6)	1 (0-6)
Duration of ADLA*	67	6.27 (4.19)	6 (1-21)	48	6.50 (3.58)	6 (2-21)	49	6.39 (4.74)	5 (1-21)	58	4.59 (2.92)	4 (1-15)
Number of days that each ADLA causes patient to miss work**	62	5.85 (4.76)	5 (1-15)	55	6.43 (3.76)	5 (2-21)	57	6.74 (4.86)	5 (1-21)	54	5.04 (3.38)	4 (1-15)
Number of entry lesions	93	0.45 (1.00)	0 (0-6)	93	1.37 (2.57)	0 (0-10)	93	0.96 (1.65)	0 (0-6)	93	0.78 (1.59)	0 (0-10)
Number of entry lesions***	23	1.82 (1.37)	1 (1-6)	32	3.97 (2.98)	3 (1-10)	33	2.70 (1.72)	2 (1-6)	30	2.43 (1.96)	2 (1-10)
Duke Depression Score	93	6.3 (3.3)	6 (0-14)	81	6.9 (3.2)	6 (1-13)	73	7.3 (3.3)	7 (1-13)	60	5.7 (2.7)	5.5 (1-11)

* Excludes respondents who reported no ALDA and respondents who reported ADLA durations of greater than 25 days.
** Excludes respondents who reported no ADLA and respondent who reported missing work for more than 25 days for each ADLA
*** Includes only respondents who reported having at least one entry lesion

Table 4: Responses to interval and ordinal questions by participants who were surveyed all 4 years

Variable	2007 YES (%)	2010 YES (%)	# from YES to NO	# from NO to YES	S value	P	mOR (95% CI)
Currently Using Effective Lymphoedema Treatments							
Elevation of the foot	19 (17.8%)	82 (76.6%)	4	67	55.90	<0.0001	16.75 (6.67, 54.08
Exercises	4 (3.7%)	84 (78.5%)	1	81	78.05	<0.0001	81 (16.05, 1638.00)
Washing	11 (10.3%)	99 (92.5%)	1	89	86.04	<0.0001	89.00 (17.67, 1798.00)
Washing, exercise, and/or elevation	27 (25.2%)	102 (95.3%)	2	77	71.20	<0.0001	38.5 (11.33, 233.4)
Leg is clean	48 (44.9%)	70 (65.4%)	7	29	13.44	0.0002	4.14 (1.88, 10.21)

Currently Using Ineffective/Harmful Lymphoedema Treatments							
Applying herbs	24 (22.4%)	2 (1.9%)	22	0	22.00	<0.0001	0.0 (0.0, 0.15)
Drinking herbs	13 (12.2%)	0 (0%)	13	0	NA	NA	0.0 (0.0, 0.26)
Hot compress	7 (6.5%)	2 (1.9%)	5	0	5.00	0.025	0 (0, 0.65)
Scarification	8 (7.5%)	1 (0.93%)	8	1	5.44	0.020	0.13 (0.0056, 0.78)
Nothing	33 (30.8%)	3 (2.8%)	32	2	26.47	<0.0001	0.063 (0.010, 0.22)
Currently using ADLA Treatments							
Applying traditional products	26 (24.3%)	5 (4.7%)	23	2	17.64	<0.0001	0.087 (0.014, 0.32)
Drinking herbs	13 (12.2%)	1 (0.93%)	13	1	10.29	0.0013	0.077 (0.0036, 0.44)
Compress	7 (6.5%)	1 (0.93%)	6	0	6.00	0.014	0.0 (0.0, 0.85)
Ointment	15 (14.0%)	6 (5.6%)	13	4	4.76	0.029	0.31 (0.09-0.90)
Prayers	5 (4.7%)	1 (0.93%)	5	1	2.67	0.10	0.20 (0.0084-1.44)
Nothing	9 (8.4%)	6 (5.6%)	8	5	0.69	0.41	0.63 (0.19, 1.93)
Activities that Lymphoedema Symptoms Prevent Patient from Performing							
Working in the field	22 (23.4%)	24 (25.5%)	13	15	0.14	0.71	1.15 (0.54, 2.48)
Going to the market	16 (18.6%)	15 (17.4%)	9	8	0.06	0.81	0.89 (0.33, 2.36)
Sweeping	4 (6.1%)	9 (13.6%)	2	7	2.78	0.096	3.50 (0.78-24.59)
Washing	0	8 (7.6%)	0	8	8.0	0.0047	NA
Getting out of bed	0	8 (7.6%)	0	8	8.0	0.0047	NA
Fetching Water	5 (12.2%)	9 (22.0%)	3	7	1.6	0.21	2.33 (0.61, 11.11)
Going to the courtyard	3 (2.9%)	7 (6.7%)	2	6	2.0	0.16	3.00 (0.63, 21.60)
Carrying Heavy Burdens	22 (40.7%)	23 (42.7%)	15	16	0.03	0.86	1.07 (0.52, 2.19)
People from whom Patients have needed help in the past week							
Family members living with them*	49 (45.8%)	51 (47.7%)	27	29	0.07	0.79	1.07(0.63-1.83)
Family members not living with them*	28 (26.2%)	32 (29.9%)	17	21	0.42	0.52	1.24 (0.65-2.38)

Friends/Neighbors *	21 (19.6%)	25 (23.4%)	18	22	0.4	0.53	1.22(0.65 , 2.31)
Community Members*	18 (16.8%)	24 (22.4%)	16	22	0.95	0.33	1.38 (0.72, 2.67)
People who have offered patients help in the past week							
Family members living with them*	57 (53.3%)	46 (43.0%)	33	22	2.2	0.14	0.67 (0.38, 1.14)
Family members not living with them*	29 (27.1%)	24 (22.4%)	22	17	0.64	0.42	0.77 (0.40, 1.46)
Friends/Neighbors *	21 (19.6%)	4 (3.7%)	21	4	11.56	0.0007	0.19 (0.056-0.52)
Community Members*	17 (15.9%)	3 (2.8%)	17	3	9.80	0.0017	0.18 (0.041-0.55)
People who have dismissed the patient in the past week							
Family members living with them	2 (1.9%)	2 (1.9%)	2	2	0.000	1	1 (0.10, 9.61)
Family members not living with them	3 (2.8%)	4 (3.7%)	3	4	0.1429	0.71	1.33 (0.28, 7.15)
Friends/Neighbors	7 (6.5%)	8 (7.5%)	6	7	0.0769	0.78	1.17 (0.38, 3.70)
Community Members	11 (10.3%)	8 (7.5%)	10	7	0.5294	0.47	0.70 (0.25, 1.9)
*Responses of "a lot" were considered to be yes responses. Responses of "a little" or "none" were considered to be no responses							

Table 4: Results of MacNemar's Paired analyses for yes-no questions

Variable	**N**	**2007 median (min-max)**	**2010 median (min-max)**	**Sign-Rank test (S)**	**P**
Lymphoedema stage	107	3 (0-6)	3 (0-6)	-67	0.6443
Number of ADLA per year*	71	2 (0-10)	2 (0-7)	-170	0.1516
Duration of ADLA**	52	6 (1-21)	4 (1-15)	163.5	0.0466
Number of days that each ALDA cause patient to miss work**	49	5 (1-15)	4 (1-20)	38	0.63
Duke Depression Score	107	7 (0-14)	4 (0-11)	1195	<0.0001
*Includes individuals who reported no ADLA in one or both years **Excludes individuals who did not report at least one ADLA in both years and those who reported ADLA length of longer than 24 days					

Table 5: Results of Sign-Rank paired analyses for continuous and ordinal variables

Potential Confounders in Model	**OR**	**95% CI**	**Precision**	**10%?**
district, age, years since symptoms began, years since symptoms became severe, sex	3.0535	(2.1317, 4.3737)	2.2420	(GS)
age, years since symptoms began, years since symptoms became severe, sex	2.9332	(2.0911, 4.1148)	2.0237	YES
years since symptoms began, years since symptoms became severe, sex	2.8976	(2.0869, 4.0232)	1.9363	YES
years since symptoms began, sex	**2.9338**	**(2.1481, 4.0068)**	**1.8587**	**YES**
years since symptoms began	2.9606	(2.1671, 4.0443)	1.8771	YES
Year is considered to be ordinal (levels 0-3) and all models contain interaction between year and years since symptoms began (3 categories)				

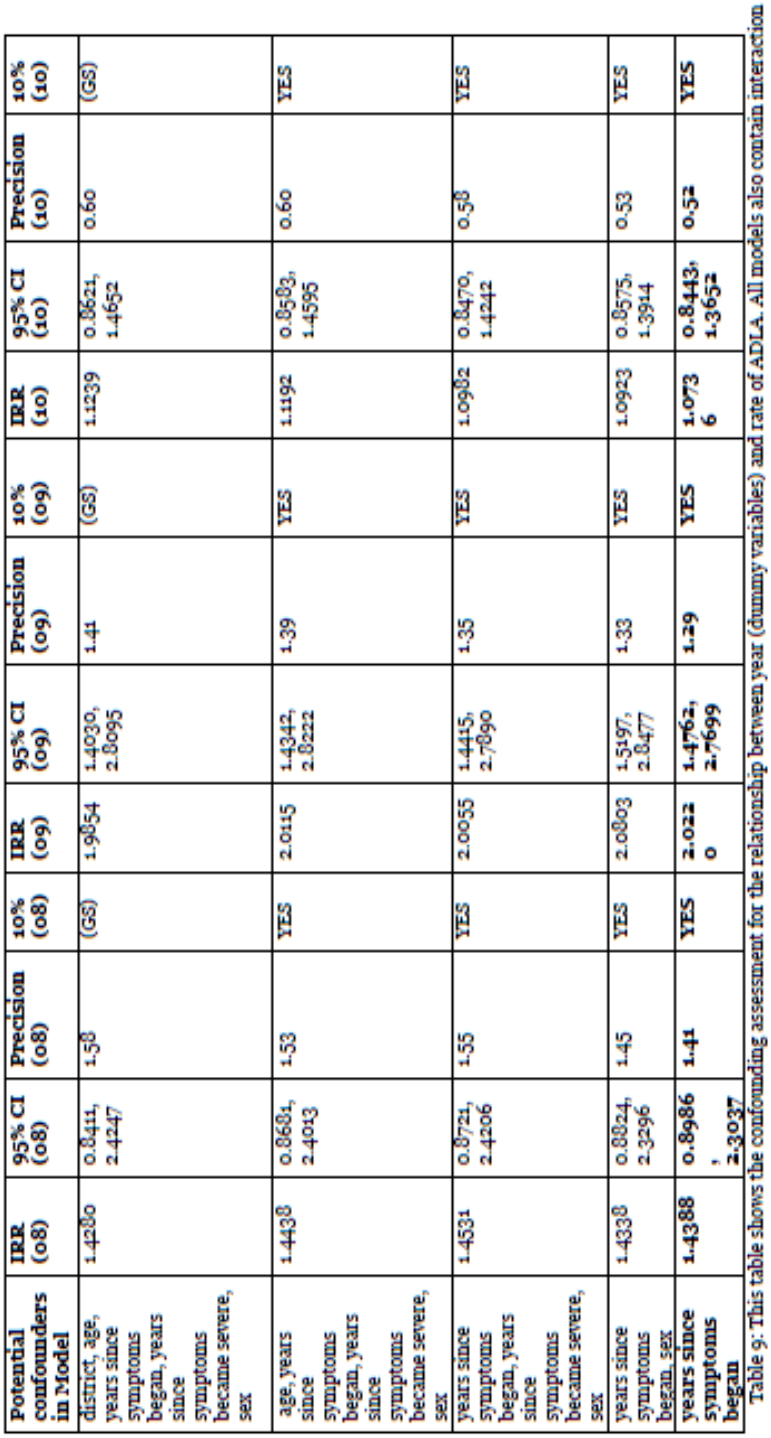
Table 6: Confounding assessment for the relationship between year and proportion of respondents who reported use of at least one appropriate treatment

Correlation Structure	QIC	Empirical SE of Yearnew	Model-Based SE of Yearnew	Difference
Stationary (3-dep)	476.0401	0.1590	0.1529	0.0061
Autoregressive (1)	476.0453	0.1589	0.1521	0.0068
Unstructured	476.2536	0.1561	0.1511	0.005
Exchangeable	476.1276	0.1598	0.1439	0.0159

Table 7: Correlation structure assessment for the final model of the relationship between year and proportion of respondents reporting use of at least one appropriate lymphoedema treatment

CONTRAST	SYMPTOMS BEGAN LESS THAN 10 YEARS AGO		SYMPTOMS BEGAN 10-30 YEARS AGO		SYMPTOMS BEGAN MORE THAN 30 YEARS AGO	
	OR	95% CI	OR	95% CI	OR	95% CI
2007 vs. 2008	8.83	3.86, 20.20	2.93	2.15, 4.01	2.81	1.78, 4.44
2007 vs. 2009	78.04	14.93, 407.93	8.61	4.61, 16.05	7.92	3.18, 19.74
2007 vs. 2010	689.39	57.69, 8239.72	25.25	9.91, 64.32	22.29	5.67, 87.74

Table 8: Results of the final model of the relationship between year and proportion of respondents reporting use of at least one appropriate lymphoedema treatment



Potential confounders in Model	IRR (08)	95% CI (08)	Precision (08)	10% (08)	IRR (09)	95% CI (09)	Precision (09)	10% (09)	IRR (10)	95% CI (10)	Precision (10)	10% (10)
district, age, years since symptoms began, years since symptoms became severe, sex	1.4280	0.8411, 2.4247	1.58	(GS)	1.9854	1.4030, 2.8095	1.41	(GS)	1.1239	0.8621, 1.4652	0.60	(GS)
age, years since symptoms began, years since symptoms became severe, sex	1.4438	0.8681, 2.4013	1.53	YES	2.0115	1.4342, 2.8222	1.39	YES	1.1192	0.8583, 1.4595	0.60	YES
years since symptoms began, years since symptoms became severe, sex	1.4531	0.872, 2.4206	1.55	YES	2.0055	1.4415, 2.7890	1.35	YES	1.0982	0.8470, 1.4242	0.58	YES
years since symptoms began, sex	1.4338	0.8824, 2.3296	1.45	YES	2.0803	1.5197, 2.8477	1.33	YES	1.0923	0.8575, 1.3914	0.53	YES
years since symptoms began	**1.4388**	**0.8986, 2.3037**	**1.41**	**YES**	**2.022 0**	**1.4762, 2.7699**	**1.29**	**YES**	**1.073 6**	**0.8443, 1.3652**	**0.52**	**YES**

Table 9: This table shows the confounding assessment for the relationship between year (dummy variables) and rate of ADLA. All models also contain interaction between year and number of years since symptoms began.

Table 9: Confounding assessment for relationship between year and rate of ADLA per year

Correlation Structure	QIC	Difference in SE 2008	Difference in SE 2009	Difference in SE 2010
Stationary (1)	-22.3903	0.0504	-0.0177	-0.0906
Autoregressive (1)	-22.3902	0.0504	-0.0177	-0.0906
Unstructured	-22.3007	0.0446	-0.011	-0.0892
Exchangeable	-22.3514	0.0525	-0.0172	-0.0897

Table 10: Correlation structure assessment for relationship between year and rate of ADLA per year

CONTRAST	SYMPTOMS BEGAN LESS THAN 10 YEARS AGO		SYMPTOMS BEGAN 10-30 YEARS AGO		SYMPTOMS BEGAN MORE THAN 30 YEARS AGO	
	IRR	95% CI	IRR	95% CI	IRR	95% CI
2007 vs. 2008	2.42	1.37, 4.26	1.44	0.90, 2.31	1.44	0.95, 2.16
2007 vs. 2009	1.15	0.82, 1.63	2.01	1.46, 2.75	0.86	0.59, 1.24
2007 vs. 2010	1.18	0.81, 1.71	1.06	0.83, 1.35	1.27	0.76, 1.13

Table 11: Results of the final model of the relationship between year and rate of ADLA per year

Figures

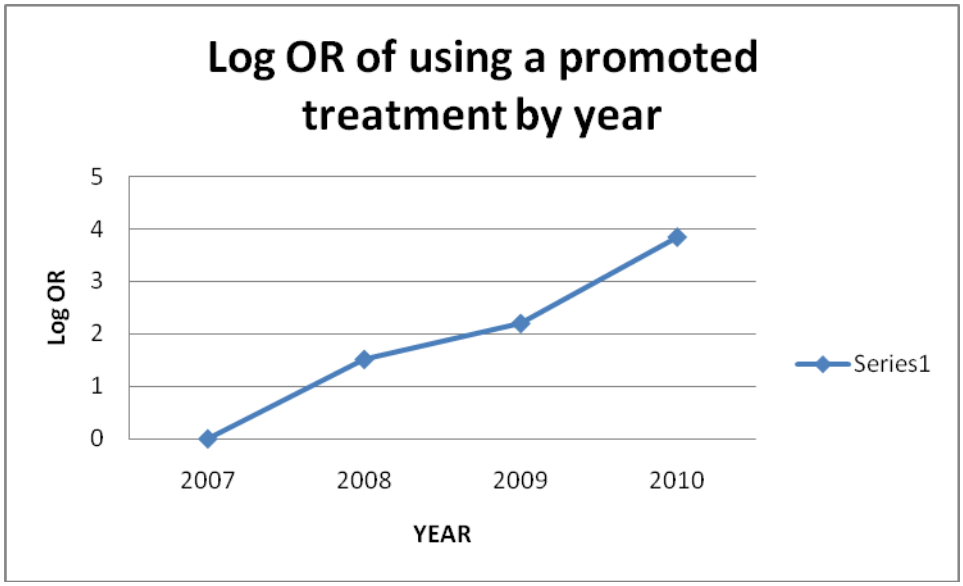


Figure1: Log-OR of using a promoted treatment by year (2007 is the reference year)

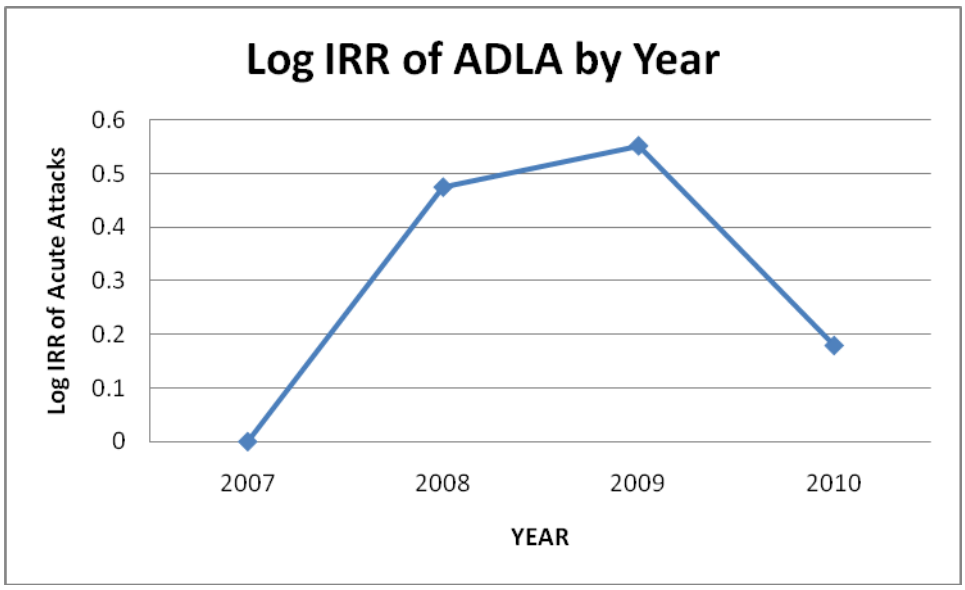


Figure 2: Log-IRR of ADLA per year (2007 is the reference year)

Appendix 1: Statistical Appendix

The variables used in all longitudinal analyses are defined as follows:

Variable Name	Definition
USETREATA	0: does not report use any of the promoted treatments 1: reports use of at least one promoted treatment
ATNUM	Number of ADLA in the past year
AGE0	1 if patient was less than 35 years old in 2007, otherwise 0
AGE1	1 if patient was over 60 years old in 2007, otherwise 0
BEGIN0	1 if patient's symptoms began less than 10 years before 2007, otherwise 0
BEGIN1	1 if patient's symptoms began in more than 30 years before 2007, otherwise 0
BAD0	1 if patient's severe symptoms began less than 10 years before 2007, otherwise 0
BAD1	1 if patient's severe symptoms began more than 20 years before 2007, otherwise 0
SEX1	1 if female, 0 if male
YEARNEW	0=2007, 1=2008, 2=2009, 3=2010
YNB	0=2010, 1=2009, 2=2008, 3=2007
Year08	1 if 2008, otherwise 0
Year09	1 if 2009, otherwise 0
Year10	1 if 2010, otherwise 0

Modeling process for proportion of patients who report use of at least one appropriate treatment

Initial multivariate model test for collinearity (CI=18.1051):

```
proc sort data=baseline5c5;
by id yearnew;
filename collin "E:\Thesis Data\collin_2011.sas";
%include collin;
proc genmod data=baseline5c5;
class id;
model usetreata=yearnew distt distk age0 age1 begin0 begin1
bad0 bad1 sex1 yearnew*distt yearnew*distk yearnew*age0 yearnew*age1
yearnew*begin0 yearnew*begin1 yearnew*bad0 yearnew*bad1 yearnew*sex1/dist=bin
link=logit type3;
repeated subject=id/ covb type=toep corrw;
ods output genmod.parminfo=parms;
ods output genmod.geercov=covdsn;
run;
%COLLIN(COVDSN=COVDSN, PROCDR=GENMOD, PARMINFO=Parms,
OUTPUT=COLIN4);
run;
```

Results of collinearity assessment:

CONDINDX	18.1051

Code for test for interaction:

```
proc genmod data=baseline5c5;
class id;
model usetreata=yearnew distt distk age0 age1 begin0 begin1
bad0 bad1 sex1 yearnew*distt yearnew*distk yearnew*age0 yearnew*age1
yearnew*begin0 yearnew*begin1 yearnew*bad0 yearnew*bad1 yearnew*sex1/dist=bin link=logit
type3;
repeated subject=id/ covb type=toep corrw;
run;
```

Results of test for interaction:

Score Statistics For Type 3 GEE Analysis			
Source	**DF**	**Chi-Square**	**Pr > ChiSq**
yearnew	1	7.41	0.0065
distt	1	0.55	0.4601
distk	1	6.18	0.0129
age0	1	2.86	0.0910
age1	1	0.66	0.4175
begin0	1	6.72	0.0095
begin1	1	0.04	0.8368
bad0	1	1.01	0.3154
bad1	1	0.45	0.5038
sex1	1	0.10	0.7460
yearnew*distt	1	0.51	0.4750
yearnew*distk	1	0.05	0.8285
yearnew*age0	1	0.06	0.8123

yearnew*age1	1	0.01	0.9242
yearnew*begin0	1	6.07	0.0138
yearnew*begin1	1	0.19	0.6666
yearnew*bad0	1	0.00	0.9824
yearnew*bad1	1	0.19	0.6643
yearnew*sex1	1	0.29	0.5920

I used backwards elimination to remove the least significant interaction term until only interaction terms significant at the 0.10 level remained. The only interaction term that was significant was yearnew*begin0. Because begin0 and begin1 are dummy variables for the same indicator, yearnew*begin0 and yearnew*begin1 were both kept in the model.

Code for the first confounding assessment:

```
proc genmod data=baseline5c5;
class id;
model usetreata=yearnew distt distk age0 age1 begin0 begin1
bad0 bad1 sex1 yearnew*begin0 yearnew*begin1/dist=bin link=logit type3;
repeated subject=id/ covb type=toep corrw;
run;
```

Results from confounding assessments are detailed in table 6. The final model after confounding assessment was:

```
proc genmod data=baseline5c5;
class id;
model usetreata=yearnew begin0 begin1 sex1 yearnew*begin0 yearnew*begin1/dist=bin
link=logit type3;
repeated subject=id/ covb type=toep corrw;
run;
```

Results of this model are as follows:

Analysis Of GEE Parameter Estimates						
Empirical Standard Error Estimates						
Parameter	**Estimate**	**Standard Error**	**95% Confidence Limits**		**Z**	**Pr > |Z|**
Intercept	0.7451	0.2549	0.2456	1.2446	2.92	0.0035

Analysis Of GEE Parameter Estimates						
Empirical Standard Error Estimates						
Parameter	**Estimate**	**Standard Error**	**95% Confidence Limits**		**Z**	**Pr > |Z|**
Yearnew	-1.0763	0.1590	-1.3880	-0.7646	-6.77	<.0001
begin0	0.7692	0.4906	-0.1924	1.7307	1.57	0.1169
begin1	0.3148	0.3981	-0.4655	1.0950	0.79	0.4291
sex1	-0.2037	0.2552	-0.7039	0.2966	-0.80	0.4249
yearnew*begin0	-1.1023	0.4510	-1.9864	-0.2183	-2.44	0.0145
yearnew*begin1	0.0415	0.2820	-0.5113	0.5943	0.15	0.8830

Score Statistics For Type 3 GEE Analysis			
Source	**DF**	**Chi-Square**	**Pr > ChiSq**
yearnew	1	39.87	<.0001
begin0	1	2.79	0.0950
begin1	1	0.65	0.4189
sex1	1	0.63	0.4279
yearnew*begin0	1	7.72	0.0055
yearnew*begin1	1	0.02	0.8833

After correlation structure assessment (see table 7), we decided to continue to use a correlation structure of stationary for the final model.

The equation for the final model is as follows:

Logit(p)x=β0+ β1year08+ β2year09+ β3year10+γ1begin0+ γ 2begin1+ γ 3sex1+δ1begin0*year08+ δ2begin0*year09+ δ3begin0*year10+ δ4begin1*year08+ δ5begin1*year09+ δ6begin0*year10

The code for the final model is as follows:

```
proc genmod data=baseline5c5 descending;
class id;
model usetreata=yearnew begin0 begin1 sex1
yearnew*begin0 yearnew*begin1/dist=bin link=logit type3;
repeated subject=id/ type=toep ;
ESTIMATE '2008 vs. 2007: <10' yearnew 1 begin0 0 begin1 0 sex1 0
yearnew*begin0 1 yearnew*begin1 0;
ESTIMATE '2009 vs. 2007: <10' yearnew 2 begin0 0 begin1 0 sex1 0
yearnew*begin0 2 yearnew*begin1 0;
ESTIMATE '2010 vs. 2007: <10' yearnew 3 begin0 0 begin1 0 sex1 0
yearnew*begin0 3 yearnew*begin1 0;
ESTIMATE '2008 vs. 2007: 10-30' yearnew 1 begin0 0 begin1 0 sex1 0
yearnew*begin0 0 yearnew*begin1 0;
ESTIMATE '2009 vs. 2007: 10-30' yearnew 2 begin0 0 begin1 0 sex1 0
yearnew*begin0 0 yearnew*begin1 0;
ESTIMATE '2010 vs. 2007: 10-30' yearnew 3 begin0 0 begin1 0 sex1 0
yearnew*begin0 0 yearnew*begin1 0;
ESTIMATE '2008 vs. 2007: >30' yearnew 1 begin0 0 begin1 0 sex1 0
yearnew*begin0 0 yearnew*begin1 1;
ESTIMATE '2009 vs. 2007: >30' yearnew 2 begin0 0 begin1 0 sex1 0
yearnew*begin0 0 yearnew*begin1 2;
ESTIMATE '2010 vs. 2007: >30' yearnew 3 begin0 0 begin1 0 sex1 0
yearnew*begin0 0 yearnew*begin1 3;
run;
```

The results of the final analysis are as follows:

Contrast Estimate Results

Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits		Chi-Square	Pr > Chi Sq
2008 vs. 2007: <10	0.8983	0.7944	0.9528	2.1786	0.4219	0.05	1.3517	3.0055	26.66	<.0001
2009 vs. 2007: <10	0.9873	0.9372	0.9976	4.3572	0.8438	0.05	2.7033	6.0111	26.66	<.0001

Contrast Estimate Results										
Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits		Chi-Square	Pr > Chi Sq
2010 vs. 2007: <10	0.9986	0.9830	0.9999	6.5358	1.2657	0.05	4.0550	9.0166	26.66	<.0001
2008 vs. 2007: 10-30	0.7458	0.6823	0.8003	1.0763	0.1590	0.05	0.7646	1.3880	45.80	<.0001
2009 vs. 2007: 10-30	0.8959	0.8219	0.9414	2.1525	0.3181	0.05	1.5291	2.7759	45.80	<.0001
2010 vs. 2007: 10-30	0.9619	0.9084	0.9847	3.2288	0.4771	0.05	2.2937	4.1639	45.80	<.0001
2008 vs. 2007: >30	0.7378	0.6406	0.8163	1.0347	0.2330	0.05	0.5780	1.4915	19.72	<.0001
2009 vs. 2007: >30	0.8879	0.7606	0.9518	2.0695	0.4660	0.05	1.1560	2.9829	19.72	<.0001
2010 vs. 2007: >30	0.9571	0.8499	0.9887	3.1042	0.6991	0.05	1.7341	4.4744	19.72	<.0001

Modeling process for the relationship between year and rate of ADLA

Code for initial multivariate model test for collinearity:

```
proc sort data=baseline5c5;
by id yearnew;
filename collin "E:\Thesis Data\collin_2011.sas";
%include collin;
proc genmod data=baseline5c5;
```

```
class id;
model atnum=year08 year09 year10 distt distk age0 age1 begin0 begin1
bad0 bad1 sex1 year08*distt year09*distt year10*distt year08*distk
year09*distk year10*distk
year08*age0 year09*age0 year10*age0 year08*age1 year09*age1 year10*age1
year08*begin0 year09*begin0 year10*begin0
year08*begin1 year09*begin1 year10*begin1
year08*bad0 year09*bad0 year10*bad0
year08*bad1 year09*bad1 year10*bad1
year08*sex1 year09*sex1 year10*sex1/dist=poisson link=log type3;
repeated subject=id/ covb type=toep corrw;
ods output genmod.parminfo=parms;
ods output genmod.geercov=covdsn;
run;
%COLLIN(COVDSN=COVDSN, PROCDR=GENMOD, PARMINFO=Parms, OUTPUT=COLIN4);
run;
```

CONDINDX	54.3351

Code for second test for collinearity (removing interaction between district and year):

```
proc sort data=baseline5c5;
by id yearnew;
filename collin "E:\Thesis Data\collin_2011.sas";
%include collin;
proc genmod data=baseline5c5;
class id;
model atnum=year08 year09 year10 distt distk age0 age1 begin0 begin1
bad0 bad1 sex1
year08*age0 year09*age0 year10*age0 year08*age1 year09*age1 year10*age1
year08*begin0 year09*begin0 year10*begin0
year08*begin1 year09*begin1 year10*begin1
year08*bad0 year09*bad0 year10*bad0
year08*bad1 year09*bad1 year10*bad1
year08*sex1 year09*sex1 year10*sex1/dist=poisson link=log type3;
repeated subject=id/ covb type=toep corrw;
ods output genmod.parminfo=parms;
ods output genmod.geercov=covdsn;
run;
%COLLIN(COVDSN=COVDSN, PROCDR=GENMOD, PARMINFO=Parms, OUTPUT=COLIN4);
run;
```

CONDINDX	30.9668

Code for third test of collinearity (removing interaction between bad0/bad1 and year):

```
proc sort data=baseline5c5;
by id yearnew;
filename collin "E:\Thesis Data\collin_2011.sas";
%include collin;
```

```
proc genmod data=baseline5c5;
class id;
model atnum=year08 year09 year10 distt distk age0 age1 begin0 begin1
bad0 bad1 sex1
year08*age0 year09*age0 year10*age0 year08*age1 year09*age1 year10*age1
year08*begin0 year09*begin0 year10*begin0
year08*begin1 year09*begin1 year10*begin1
year08*sex1 year09*sex1 year10*sex1/dist=poisson link=log type3;
repeated subject=id/ covb type=toep corrw;
ods output genmod.parminfo=parms;
ods output genmod.geercov=covdsn;
run;
%COLLIN(COVDSN=COVDSN, PROCDR=GENMOD, PARMINFO=Parms, OUTPUT=COLIN4);
run;
```

CONDINDX	21.2354

Code for first test for interaction:

```
proc genmod data=baseline5c5;
class id ynb;
model atnum=ynb distt distk age0 age1 begin0 begin1
bad0 bad1 sex1 ynb*age0 ynb*age1 ynb*begin0
ynb*begin1 ynb*sex1 /dist=poisson link=log type3;
repeated subject=id/ covb type=toep corrw;
run;
```

Results of first test for interaction:

Score Statistics For Type 3 GEE Analysis			
Source	**DF**	**Chi-Square**	**Pr > ChiSq**
Ynb	3	4.82	0.1858
Distt	1	0.37	0.5441
Distk	1	0.07	0.7914
age0	1	0.00	0.9743
age1	1	1.14	0.2865
begin0	1	0.38	0.5397
begin1	1	2.02	0.1554
bad0	1	0.82	0.3653

Score Statistics For Type 3 GEE Analysis			
Source	**DF**	**Chi-Square**	**Pr > ChiSq**
bad1	1	0.28	0.5980
sex1	1	0.75	0.3859
age0*ynb	3	0.42	0.9362
age1*ynb	3	3.07	0.3811
begin0*ynb	3	4.79	0.1880
begin1*ynb	3	7.33	0.0621
sex1*ynb	3	1.56	0.6688

I used backwards elimination to remove non-significant interaction terms one at a time. The only interaction term that was significant was yearnew*begin1. Because begin0 and begin1 are dummy variables for the same indicator, yearnew*begin0 and yearnew*begin1 were both kept in the model.

Code for first confounding assessment:

```
proc genmod data=baseline5c5;
class id ynb;
model atnum=ynb distt distk age0 age1 begin0 begin1
bad0 bad1 sex1 ynb*begin0
ynb*begin1 /dist=poisson link=log type3;
repeated subject=id/ covb type=toep corrw;
run;
```

Results of confounding assessment are detailed in table 9. The code for the model after confounding assessment is as follows:

```
proc genmod data=baseline5c5;
class id ynb;
model atnum=ynb begin0 begin1
 ynb*begin0
ynb*begin1 /dist=poisson link=log type3;
repeated subject=id/ covb type=un corrw modelse;
run;
```

Correlation structure assessment is detailed in table 10. For the final model, a correlation structure of unstructured was used. The equation for the final model is as follows:

Logit(p)x=β0+ β1year08+ β2year09+ β3year10+γ1begin0+ γ 2begin1+δ1begin0*year08+ δ2begin0*year09+ δ3begin0*year10+ δ4begin1*year08+ δ5begin1*year09+ δ6begin0*year10

The code for the final model is as follows:

```
proc genmod data=baseline5c5;
class id;
model atnum=year08 year09 year10 begin0 begin1
 year08*begin0    year09*begin0 year10*begin0
year08*begin1  year09*begin1 year10*begin1
/dist=poisson link=log type3;
ESTIMATE '2008 vs. 2007: <10' year08 1 year09 0 year10 0 begin0 1
begin1 0 year08*begin0 1 year09*begin0 0 year10*begin0 0 year08*begin1
0 year09*begin1 0 year10*begin1 0;
ESTIMATE '2009 vs. 2007: <10' year08 0 year09 1 year10 0 begin0 1
begin1 0 year08*begin0 0 year09*begin0 1 year10*begin0 0 year08*begin1
0 year09*begin1 0 year10*begin1 0;
ESTIMATE '2010 vs. 2007: <10' year08 0 year09 0 year10 1 begin0 1
begin1 0 year08*begin0 0 year09*begin0 0 year10*begin0 1 year08*begin1
0 year09*begin1 0 year10*begin1 0;
ESTIMATE '2008 vs. 2007: 10-30' year08 1 year09 0 year10 0 begin0 0
begin1 0 year08*begin0 0 year09*begin0 0 year10*begin0 0 year08*begin1
0 year09*begin1 0 year10*begin1 0;
ESTIMATE '2009 vs. 2007: 10-30' year08 0 year09 1 year10 0 begin0 0
begin1 0 year08*begin0 0 year09*begin0 0 year10*begin0 0 year08*begin1
0 year09*begin1 0 year10*begin1 0;
ESTIMATE '2010 vs. 2007: 10-30' year08 0 year09 0 year10 1 begin0 0
begin1 0 year08*begin0 0 year09*begin0 0 year10*begin0 0 year08*begin1
0 year09*begin1 0 year10*begin1 0;
ESTIMATE '2008 vs. 2007: >30' year08 1 year09 0 year10 0 begin0 0
begin1 1 year08*begin0 0 year09*begin0 0 year10*begin0 0 year08*begin1
1 year09*begin1 0 year10*begin1 0;
ESTIMATE '2009 vs. 2007: >30' year08 0 year09 1 year10 0 begin0 0
begin1 1 year08*begin0 0 year09*begin0 0 year10*begin0 0 year08*begin1
0 year09*begin1 1 year10*begin1 0;
ESTIMATE '2010 vs. 2007: >30' year08 0 year09 0 year10 1 begin0 0
begin1 0 year08*begin0 0 year09*begin0 0 year10*begin0 0 year08*begin1
0 year09*begin1 0 year10*begin1 1;
repeated subject=id/ covb type=un corrw modelse;
run;
```

The results of the contrasts in the final model are as follows:

Contrast Estimate Results										
Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits		Chi-Square	Pr > ChiSq
2008 vs. 2007: <10	2.4204	1.3738	4.2643	0.8839	0.2890	0.05	0.3176	1.4503	9.36	0.0022

Contrast Estimate Results										
Label	Mean Estimate	Mean Confidence Limits		L'Beta Estimate	Standard Error	Alpha	L'Beta Confidence Limits		Chi-Square	Pr > ChiSq
2009 vs. 2007 : <10	1.1533	0.8172	1.6276	0.1426	0.1758	0.05	-0.2019	0.4871	0.66	0.4171
2010 vs. 2007 : <10	1.1761	0.8071	1.7137	0.1622	0.1921	0.05	-0.2143	0.5387	0.71	0.3985
2008 vs. 2007 : 10-30	1.4416	0.9017	2.3050	0.3658	0.2394	0.05	-0.1035	0.8351	2.33	0.1266
2009 vs. 2007 : 10-30	2.0067	1.4638	2.7511	0.6965	0.1610	0.05	0.3810	1.0120	18.72	<.0001
2010 vs. 2007 : 10-30	1.0615	0.8333	1.3522	0.0597	0.1235	0.05	-0.1824	0.3018	0.23	0.6289
2008 vs. 2007 : >30	1.4355	0.9537	2.1606	0.3615	0.2086	0.05	-0.0474	0.7704	3.00	0.0831
2009 vs. 2007 : >30	0.8582	0.5922	1.2437	-0.1529	0.1893	0.05	-0.5238	0.2181	0.65	0.4193
2010 vs. 2007 : >30	1.2702	0.7582	2.1279	0.2392	0.2633	0.05	-0.2768	0.7552	0.83	0.3636

Results of the final model are detailed in table 11.

Appendix 2: Emory Institutional Review Board Approval

EMORY UNIVERSITY | Institutional Review Board

April 18, 2011

Kira Harvey
Emory University
Rollins School of Public Health
1518 Clifton Road
Atlanta, GA 30322

RE: Determination: No IRB Review Required
Epidemiology Thesis
PI: Kira Harvey

Dear Ms. Harvey:

Thank you for requesting a determination from our office about the above-referenced project. Based on our review of the materials you provided, we have determined that it does not require IRB review because it does not meet the definitions of "research" involving "human subjects" or the definition of "clinical investigation" as set forth in Emory policies and procedures and federal rules, if applicable.

45 CFR Section 46.102(d) defines "Research" as follows:

> Research means a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. Activities which meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes.

Based on the information included in the submission, the purpose of this project is to evaluate the impact of the National Lymphoedema Management Programme on the behavior and physical, psychological, and social well-being of lymphatic filariasis patients in Togo. This study's aim may best be identified as program evaluation, and the results are not expected to be generalizable. Additionally, the dataset you received from the Centers for Disease Control contains no identifiers. As such, the IRB has determined that this study does not constitute "research" under the foregoing definition, nor does it involve the use of "human subjects" since the data you receive will not be identifiable.

This determination could be affected by substantive changes in the study design, subject populations, or identifiability of data. If the project changes in any substantive way, please contact our office for clarification.

Sincerely,

Tom Penna, MTS
IRB Analyst Assistant
This letter has been digitally signed

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