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Impact of Community-Based Lymphedema Management on Perceived Disability among Patients with Lymphatic Filariasis in Orissa State, India

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Abstract

Background: Lymphatic filariasis (LF) infects approximately 120 million people worldwide. As many as 40 million have symptoms of LF disease, including lymphedema, elephantiasis, and hydrocele. India constitutes approximately 45% of the world’s burden of LF. The Indian NGO Church’s Auxiliary for Social Action (CASA) has been conducting a community-based lymphedema management program in Orissa State since 2007 that aims to reduce the morbidity associated with lymphedema and elephantiasis. The objective of this analysis is to evaluate the effects of this program on lymphedema patients’ perceived disability.

Methodology/Principal Findings: For this prospective cohort study, 370 patients ≥14 years of age, who reported lymphedema lasting more than three months in one or both legs, were recruited from villages in the Bolagarh sub-district, Khurda District, Orissa, India. The World Health Organization Disability Assessment Schedule II was administered to participants at baseline (July, 2009), and then at regular intervals through 24 months (July, 2011), to assess patients’ perceived disability. Disability scores decreased significantly (p<0.0001) from baseline to 24 months. Multivariable analysis using mixed effects modeling found that employment and time in the program were significantly associated with lower disability scores after two years of program involvement. Older age, female gender, the presence of other chronic health conditions, moderate (Stage 3) or advanced (Stage 4–7) lymphedema, reporting an adenolymphangitis (ADL) episode during the previous 30 days, and the presence of inter-digital lesions were associated with higher disability scores. Patients with moderate or advanced lymphedema experienced greater improvements in perceived disability over time. Patients participating in the program for at least 12 months also reported losing 2.5 fewer work days per month (p<0.001) due to their lymphedema, compared to baseline.

Significance: These results indicate that community-based lymphedema management programs can reduce disability and prevent days of work lost. These effects were sustained over a 24 month period.

Introduction

Lymphatic filariasis (LF) is a parasitic infection that leads to damage of the lymphatic system, causing lymphedema of the legs, arms, breast, or genitals. These symptoms affect an estimated 40 million people, making LF the second-leading cause of disability globally [1,2]. Despite remarkable progress toward the interruption of LF transmission [3], less attention has been paid to LF morbidity management and disability prevention, which remain critical problems in many endemic areas [4].

Though filarial infection causes initial lymphatic dysfunction, development and progression of lymphedema is thought to result from recurrent episodes of secondary bacterial infections, known as adenolymphangitis (ADL). Patients with lymphatic damage are at increased risk for ADL episodes due to poor lymphatic drainage and predisposition to interdigital fungal infections, which can serve as a portal of entry for pathogenic bacteria [5]. ADL episodes are characterized by pain, swelling, and inflammation of the affected extremity, often accompanied by fever or chills. These episodes further damage lymphatic vessels and worsen lymphatic dysfunction, leading to an increased risk for additional ADL episodes [5].
Author Summary

Lymphatic filariasis (LF) is the world’s second-leading cause of disability and causes limb lymphedema and elephantiasis in up to 15 million people and lymphedema or hydrocele in over 40 million people, worldwide. A massive global effort has been undertaken to eliminate LF as a public health problem. LF elimination is based on two pillars: (1) interruption of transmission and (2) treatment of clinical disease among those already affected. The Indian NGO, Church’s Auxiliary for Social Action (CASA), has been providing community-based treatment of lymphedema in Khurda District, Orissa State, India, since 2007. We evaluated the impact of this treatment program on the participating patients’ perceived disability using the WHO Disability Assessment Schedule II (WHO-DAS II). After two years of enrollment in the program, patients had significantly lower levels of perceived disability. We found that being employed and time enrolled in the program were associated with significant reductions in disability scores. Compared to baseline, patients enrolled in the program for at least 12 months reported 2.5 fewer days of work lost in the previous 30 days due to their lymphedema. These findings indicate that participation in a community-based lymphedema management program can reduce patients’ disability and prevent days of work lost due to lymphedema.

While LF-associated lymphedema cannot be completely cured, low-cost, effective approaches to morbidity management are available for lymphedema patients [6,7]. Proper care of lymphedema, known as lymphedema management, has been shown to be effective in preventing disease progression, reducing limb swelling, and reducing the frequency of ADL episodes [6–8]. Lymphedema management includes regular limb washing, appropriate exercise, elevation of the affected limb, early treatment of bacterial and fungal infections, and use of proper footwear [5].

Morbidity control is of special concern in India, where an estimated 59 million people are infected with the parasites that cause lymphatic filariasis, approximately 19.6 million of whom exhibit symptoms of lymphedema, elephantiasis, or hydrocele [9]. LF predominately affects the poorest segments of India’s population, and the associated morbidity and disability are compounded by stigmatization, strict caste and gender roles, and a lack of access to healthcare [10–12].

Since 2007, the Indian non-governmental organization (NGO) Church’s Auxiliary for Social Action (CASA), has been providing community-based treatment of lymphedema in Orissa State, India (Figure 1) [13]. The program currently serves more than 20,000 lymphedema patients and their families through a network of village volunteers, who are trained to provide home-based care and instruction in lymphedema management techniques.

While previous studies have demonstrated improvements in patient quality of life and a reduction in ADL episodes after beginning lymphedema management, most have assessed patients over relatively short periods of time (≤1 year) and on a smaller scale [14,15]. The objective of this study, therefore, was to evaluate the longer-term impact of a large-scale, community-based lymphedema management program on perceived disability and productivity among lymphedema patients using a validated disability-assessment tool [16].

Methods

Ethics Statement

This project was submitted for human subjects review to the Center for Global Health at the Centers for Disease Control and Prevention (CDC), Atlanta, Georgia, USA. The project was determined to be program evaluation under CDC policy prior to the implementation of the survey. Permission for the survey was obtained from the Orissa State Department of Health and Family Welfare. Participants were asked to give their written consent prior to participation. For those unable to write, consent was documented by recording the person’s fingerprint or marking the signature line with an ‘X’ and by countersignature of survey personnel. For participants under 18 years of age, verbal consent of a parent or guardian was also obtained. Consent procedures were approved by CDC and the Orissa State Department of Health and Family Welfare.

Study Area

Khurda District, Orissa State, India, is located near India’s east coast on the northern portion of the Bay of Bengal (Figure 1), and contains the state capitol of Bhubhaneswar. Khurda District has a population of approximately 1.9 million and is highly endemic for lymphatic filariasis caused by Wuchereria bancrofti, with surveys from 2001–2005 estimating between 22,500 and 235,000 microfilaria-infected persons [17–20]. CASA provides services to >20,000 lymphedema patients in the Orissa State. Study patients were enrolled from randomly selected villages in Bolagarh, one sub-district of Khurda district. The map shown in Figure 1 was generated by ArcMAP 10.1 software (ESRI, Redlands, California, USA), using shapefiles downloaded from DIVA-GIS (http://www.diva-gis.org/gdata).

Study Design

The study was conducted from July 2009–July 2011 in 30 villages in Bolagarh sub-district. Villages were eligible for inclusion in the study if they had not yet been enrolled in the lymphedema management program, and were not located in the immediate vicinity of a village that had already been enrolled in the program. Lymphedema patients were selected based on a house-to-house morbidity census conducted by CASA in 2003 and repeated prior to the start of the program. Patients were eligible for the study if they were ≥14 years of age and had reported lower leg swelling of at least three months duration. Patients with lymphedema of the breast, arm, or genitals (in the absence of lower-limb lymphedema) were not eligible for participation in the study.

The study was powered to detect a 5% decrease in the frequency of ADL episodes, with a 15% drop-out rate, from baseline to 24 months post-enrollment in the lymphedema management program, with an alpha of 0.05.

In-person interviews with participating patients were conducted by trained local interviewers in Oriya, the local language. Interviews included questions regarding general demographic information, history of lymphedema, understanding of and compliance with lymphedema management, frequency of ADL episodes, and access to care.

Lymphedema patients were evaluated prior to enrollment in the lymphedema management program, and again at 1 month, 2 months, 3 months, 6 months, 12 months, 18 months, and 24 months after enrollment in the program. Evaluation included a physical examination of the affected extremity and administration of a pre-tested questionnaire. Due to logistics issues, the 18 month data collection was not performed on time and therefore is not included in this analysis.

The physical assessment of each patient was conducted by both a trained interviewer and a supervisor. Both the interviewer and the supervisor performed independent staging of the leg(s) and photographs were taken of the affected limb(s). Staff used the 7-stage classification system developed by Dreyer and colleagues [5] to stage patients’ degree of lymphedema. Where staging was inconsistent between the interviewer and supervisor, or with prior or
subsequent staging, photographs were independently reviewed by two physicians with extensive LF experience (P. Budge and L. Fox), and discrepancies were resolved. For this analysis, stages were combined into three categories: early lymphedema (stages 1–2), moderate lymphedema (stage 3), and advanced lymphedema (stages 4–7). An adenolymphangitis (ADL) episode was defined as a patient self-report of two or more of the following symptoms: redness, pain, or swelling of the leg or foot, with or without the presence of fever or chills, during any point in the previous 30 days.

**WHO Disability Assessment Schedule II**

The World Health Organization Disability Assessment Schedule II (WHO DAS II) was administered to patients at each interview. The WHO-DAS II survey, created by the World Health Organization, is designed to assess daily function across six broad categories, or domains, including cognition, mobility, self-care, getting along with others, life activities, and participation in society [16]. The instrument measures an individual’s perception of their disability through a series of questions scored on a 5-point scale ranging from 1 (“No difficulty”) to 5 (“Extreme difficulty or cannot do”). The questions are based on the interviewee’s perception of their experiences over the last 30 days. Taken together, these scores provide an overall assessment of total perceived disability, with higher scores corresponding to higher levels of perceived disability. This analysis used simple (un-weighted) scoring of the WHO-DAS II domains to calculate an overall disability score.

**Figure 1. Map of India.** The location of Orissa state (shaded gray) and Khurda District (shaded black) are indicated. doi:10.1371/journal.pntd.0002100.g001
Data Analysis

Data were independently dual-entered into Epi Info 7, (Stone Mountain, 2008) and then checked for inconsistencies. Data cleaning and analysis were performed in SAS 9.3 (Cary, North Carolina, USA). Paired T-tests were used to examine perceived disability changes over time and changes in mean days of work lost due to lymphedema. These paired analyses compared the disability or domain score at each time point to the same patients’ scores at baseline—the baseline scores of patients not present at any given assessment were not included in that assessment’s comparison. Mixed effects model linear regression was used to identify factors associated with changes in disability scores over time, taking into account correlations in the data over the entire 24 month study period. All variables that were statistically significant (P<0.05) on univariate analysis were included in the final predictive model, as were important demographic variables. Variables were checked for co-linearity before their inclusion in the final model.

Sensitivity Analyses

To examine the effect of loss to follow-up, sensitivity analyses using the methods listed above, but excluding those patients not present at study end, were performed.

Results

Demographic Characteristics

A total of 457 patients were selected from 30 villages. Initially, 375 (82%) met the inclusion criteria and agreed to participate in the study. Five patients were subsequently excluded from analysis, due to lack of lymphedema on examination (n = 2), failure to meet the age criteria (n = 1), or mislabeling of survey forms (n = 2). Fifty-four (14.6%) patients were lost to follow-up during the 24 month study period. Over the course of the study, reasons for non-participation at any particular assessment were absence from the village at the time of the assessment (70%), refusal (7%), illness (6%), or death (17%). In total, the study encompassed over 658 person-years of observation time (baseline to time of last follow-up).

At enrollment participants averaged 57.2 years of age, and the majority were women (218, 59%) (Table 1). Most participants (298, 81%) were married, and only 75 (20%) had more than a primary school education. Approximately half of the study population (49%) identified “Homemaker/Housekeeper” as their primary occupation, while 57 (17%) reported being unemployed or retired. More than 40% (162) of patients reported at least one chronic health condition. The most common co-morbidities were high blood pressure (62, 16.7%), and stomach problems (66, 17.8%).

Table 1. Characteristics of patients enrolled in lymphedema management: July 2009–July 2011.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline (N = 370)</th>
<th>12 months (N = 320)</th>
<th>24 months (N = 315)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (Mean, SD)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (Mean, SD)</td>
<td>57.15</td>
<td>13.94</td>
<td>57.07</td>
<td>13.62</td>
</tr>
<tr>
<td>Female Gender</td>
<td>218</td>
<td>58.92</td>
<td>190</td>
<td>59.19</td>
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<tr>
<td>Married</td>
<td>298</td>
<td>80.54</td>
<td>256</td>
<td>80</td>
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<tr>
<td>Higher than Primary Education</td>
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<td>20.33</td>
<td>61</td>
<td>19</td>
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<td><strong>Work</strong></td>
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<td></td>
</tr>
<tr>
<td>Homemaker/Housekeeper</td>
<td>165</td>
<td>49.25</td>
<td>148</td>
<td>50.17</td>
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<tr>
<td>Unemployed/Retired</td>
<td>57</td>
<td>17.01</td>
<td>47</td>
<td>15.93</td>
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<tr>
<td>Work or Study</td>
<td>113</td>
<td>33.73</td>
<td>100</td>
<td>33.9</td>
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<tr>
<td><strong>Caste</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>General Caste</td>
<td>147</td>
<td>39.73</td>
<td>127</td>
<td>39.56</td>
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<tr>
<td>Other Backward</td>
<td>175</td>
<td>47.3</td>
<td>153</td>
<td>47.66</td>
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<tr>
<td>Scheduled Caste</td>
<td>28</td>
<td>7.57</td>
<td>25</td>
<td>7.79</td>
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<tr>
<td>Scheduled Tribe</td>
<td>20</td>
<td>5.41</td>
<td>16</td>
<td>4.98</td>
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<tr>
<td><strong>Any Chronic Health Condition</strong></td>
<td>162</td>
<td>43.78</td>
<td>136</td>
<td>42.37</td>
</tr>
<tr>
<td><strong>Co-morbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Blood Pressure</td>
<td>62</td>
<td>16.76</td>
<td>65</td>
<td>20.25</td>
</tr>
<tr>
<td>Diabetes</td>
<td>12</td>
<td>3.24</td>
<td>10</td>
<td>3.12</td>
</tr>
<tr>
<td>Cancer</td>
<td>2</td>
<td>0.54</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Heart Problems</td>
<td>8</td>
<td>2.16</td>
<td>6</td>
<td>1.87</td>
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<tr>
<td>Stomach Problems</td>
<td>66</td>
<td>17.84</td>
<td>62</td>
<td>19.31</td>
</tr>
<tr>
<td>Stage of Most-Effected Leg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (Stage 1-2)</td>
<td>184</td>
<td>49.73</td>
<td>177</td>
<td>55.31</td>
</tr>
<tr>
<td>Moderate (Stage 3)</td>
<td>133</td>
<td>35.95</td>
<td>92</td>
<td>28.75</td>
</tr>
<tr>
<td>Advanced (Stage 4-6)</td>
<td>53</td>
<td>14.32</td>
<td>51</td>
<td>15.94</td>
</tr>
<tr>
<td>Years with lymphedema</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean, SD</td>
<td>25.48</td>
<td>16.04</td>
<td>25.77</td>
<td>16.37</td>
</tr>
<tr>
<td>Bilateral Lymphedema</td>
<td>124</td>
<td>33.51</td>
<td>109</td>
<td>34.06</td>
</tr>
</tbody>
</table>

*Denotes the p-value for the difference between baseline and 24 months.

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chronic health condition other than lymphedema at one or more
time points during the study. The most commonly reported
chronic conditions were gastrointestinal problems (18%) and high
blood pressure (17%).

The majority of patients had lymphedema classified as “early”
(Stage 1–2) (50%), or “moderate” (Stage 3) (36%). Only 53 (14%)
of patients had lymphedema classified as “advanced” (Stages 4–7).
Patients reported having experienced lymphedema symptoms for
an average of 25.5 years (range: 1.0–75.0 years). One hundred
twenty-four (34%) patients reported bilateral lymphedema. There
were no statistically significant differences in demographic
characteristics between baseline and the twenty-four month
assessment except that significantly more patients were classified
as having early lymphedema at 24 months as compared to baseline
(p = 0.0155). A subset analysis of the 316 patients present at 24
months revealed that 55 of these patients (17%) were in a lower
stage category at study end compared to baseline, while 20 (6%)
were in a higher stage category (data not shown). Among the 54
patients lost to follow-up by study end, 32 (59%) had early
lymphedema, 15 (28%) had moderate lymphedema, and 7 (13%)
had advanced lymphedema (data not shown). This did not vary
significantly from the baseline characteristics of those who
remained in the study.

Perceived Disability Scores over Time

Composite disability scores from the WHO-DAS II question-
naire decreased from an average score of 66.2 at baseline to 60.4
at 24 months (p<0.0001), a decline of more than 9%. This reflects
significant and sustained reduction in each of the six WHO-DAS
II component domains, with the exception of mobility and self-
care (Figure 2). Patients reported a 13% decrease in cognitive
disability from baseline to twenty-four months post-enrollment
(p<0.0001). Disability in the domain “Getting Along with Others”
declined 12% (p<0.005), while disability in life activities decreased
7% (p = 0.0046). Difficulty participating in society decreased 11%
(p<0.0001) from baseline to twenty-four months. Disability in
mobility also decreased slightly during the follow-up period (4%),
as did scores for self-care (6%), though neither of these declines
was statistically significant.

After stratifying by lymphedema category, patients with the
most advanced lymphedema (Stages 4–7) saw the largest
reductions in overall disability scores (Figure 3). Scores in this
group fell approximately 13% between baseline and 24 months
(p = 0.0044). Patients with moderate lymphedema (Stage 3)
reported a 10% drop in disability over 24 months (p = 0.0011),
while patients with early stage lymphedema (Stages 1–2) experi-
cenced a smaller percent reduction in scores (5%) that did not reach
statistical significance (p = 0.0697).

Analysis of Factors Affecting Perceived Disability

A number of factors were significantly associated with total
disability score on univariate analysis (Table 2). Factors associated
with a decrease in perceived disability and lower WHO-DAS II
composite scores included having at least a primary school
education (estimate: −6.9, 95% CI: −10.4, −3.4), and being
employed as a homemaker (estimate: −5.6, 95% CI: −7.9, −3.4)
or a worker or student (estimate: −7.6, 95% CI: −10.0, −5.3).
Being currently married was also associated with a lower disability
score (estimate: −3.1, 95% CI: −5.7, −0.6). The only individual
component of lymphedema management that was significantly
associated with reduced disability levels on univariate analysis was
wearing shoes. Compared to those never wearing shoes, individ-
uals reporting always wearing shoes while outside had disability
scores 2.8 points lower (95% CI: −4.6, −1.1). When compared to
baseline measures, time in the program was also associated with
decreased disability scores for every time-point.

Factors associated with an increased disability score in
univariate analysis included belonging to the highest age quartile
(estimate: 10.9, 95% CI: 7.0, 14.8), the presence of one or more
additional chronic health problems (estimate: 7.2; 95% CI: 4.3,
10.1), moderate (estimate: 2.7; 95% CI: 0.9, 4.6) or advanced
lymphedema (estimate: 11.7; 95% CI: 8.3, 15.0), bilateral
lymphedema (estimate: 3.5; 95% CI: 0.7, 6.3), the presence of
interdigital lesions, which are fungal and bacterial infections in the
interdigital web spaces, (estimate: 5.1, 95% CI: 3.3, 6.8), and
having had an ADL episode in the previous 30 days (estimate:
11.3, 95% CI: 10.0, 13.0). The strongest predictor of perceived
disability, however, was patients’ self-reported health rating for the
past 30 days. Patients reporting “Very bad” health had scores
more than 38 points higher than those reporting “Very good”
health (estimate: 38.9, 95% CI: 33.1, 44.6).

In multivariate analysis several factors remained significantly
associated with decreased disability scores on the WHO-DAS II
(Table 2). After controlling for covariates, patients who reported
being employed as a homemaker had WHO-DAS II scores
5.7 points lower than those who were unemployed (95% CI: −8.2,
−3.3), while women scored 5.7 points lower than those who were
unemployed (95% CI: −6.8, −2.1). The individual components of lymphedema management, including
soap use, elevation of the affected limb, wearing shoes, and
antifungal cream use were not significantly associated with
disability scores after controlling for other covariates. However,
patients who reported performing leg exercises more than once
a week (but less than once a day) had scores 2.6 points lower than
patients who never performed the exercises (95% CI: −5.2, −0.1).
Time enrolled in the program was significantly associated with
decreased disability scores through 12 months of program
participation.

Risk factors for increased overall disability that remained
significant in multivariate analysis included belonging to the oldest
age quartile, female gender, the presence of other chronic health
problems, moderate or advanced lymphedema, the presence of
interdigital lesions, and having had an ADL episode in the past 30
days. Patients belonging to the oldest age quartile had scores
7.9 points higher than patients in the youngest age quartile (95% CI:
4.0, 11.7), while women scored 5.7 points higher than their
male counterparts (95% CI: 2.2, 9.3). Patients with lymphedema
stage 4 or higher scored 8.4 points higher on the WHO-DAS II
than patients with early stage lymphedema (95% CI: 5.0, 11.8).
ADL episodes had the largest effect on disability scores in our
model. Patients reporting an ADL episode in the previous 30 days
had scores 10.6 points higher than those who had not reported an
ADL episode (95% CI: 9.1, 12.2).

In a multivariate model including the predictors above as well as
patient self-reported overall health status, patient health rating
during the previous 30 days remained the largest predictor of
increased disability (data not shown). After controlling for
covariates, patients reporting “Very bad” health during the last
30 days scored approximately 33 points higher on total disability
than patients who reported “Very good” health (95% CI: 27.2,
39.4).

Days of Work Lost Due to Lymphedema

At each assessment time point, patients were asked about the
number of days of work lost in the preceding 30 days due to
lymphedema-associated disability. At baseline, patients reported
an average of 6.4 (95% CI: 5.6, 7.2) days of work lost due to
disability in the previous 30 days (Figure 4). After enrollment into
Figure 2: Mean WHO-DAS II disability scores by domain. Scores for each domain are shown as labeled; total disability is shown in the lowest panel.
doi:10.1371/journal.pntd.0002100.g002
the lymphedema management program, the average number of
days of work lost in the previous 30 days declined to 4.7 (95% CI:
4.0, 5.4) at 2 months and 2.9 (95% CI: 2.4, 3.4) at 6 months. At 24
months post-enrollment, the number of days of work lost remained
significantly lower than baseline, at 3.9 (95% CI: 3.2, 4.6).

Stratified by lymphedema stage, patients with advanced
lymphedema reported missing more days of work due to their
lymphedema in the previous 30 days at baseline than patients with
early stage lymphedema (5.3 days vs. 10.4 days, p = 0.0265) (Data
not shown). However, patients with advanced lymphedema also
saw the greatest reduction in days of work lost at 24 months, with a
44% decline from 10.4 to 5.9 days (p = 0.0083). Patients with
moderate stage lymphedema also saw a significant decrease in
days of work lost from 6.2 to 4.5 days. (28%, p = 0.0439).

Sensitivity Analysis

The mixed effects model used to analyze factors associated with
a change in disability score and the paired comparisons of
perceived disability (comparing each individual’s score to their
corresponding baseline score) account for missing data, so
exclusion of the 54 patients not present at study end should have
little effect on the reported outcomes. To verify this, the analyses
were repeated including only those 316 patients present at study
end. This did not change the significance of any observed
differences in perceived disability, and in all cases exaggerated
the magnitude of the difference (data not shown). Excluding the 54
patients not present at study end also made no difference in
determining which variables were significant in the multivariate
analysis, except to make the association between the 24 month
assessment (variable “Time” in Table 1) reach statistical signifi-
cance (data not shown).

Discussion

This study found that patients enrolled in a community-based
lymphedema management program experienced less disability in
almost every domain of the WHO-DAS II, including participation
in community life and cognition, compared to baseline. These
benefits were sustained through two years of follow-up. These
results are consistent with other studies which have demonstrated
decreased disability, fewer ADL episodes, and improved quality of
life amongst lymphedema patients involved in lymphedema
management programs [21–23].

After controlling for other predictors, including time in the
program, the best predictor of patient perceived disability was self-
reported health status in the previous 30 days. Worsening reported
health status corresponded with increases in WHO-DAS II
composite disability scores at every time point in the survey,
indicating that self-reported health status may serve as a simple
proxy measure for composite perceived disability among lymph-
edema patients.

Other significant contributors to increases in composite
disability scores were older age and advanced lymphedema.
Though this study found that the oldest patients had the highest
disability scores at both baseline and 24 months after enrollment,
these patients also experienced the greatest percent declines in
these scores over their two years in the program. This same
pattern held true for patients with the most advanced lymphedema
(Stages 4–7), who experienced greater percent declines in their
composite disability scores than patients with less advanced
lymphedema (Stage 1–2). These findings suggest that simple,
low-cost interventions, such as those used in this community-based
lymphedema management program, can significantly impact
perceived levels of disability for even the oldest and most advanced
lymphedema patients, even in the absence of more intensive and
costly interventions such as bandaging, massage, and IV antibi-
otics.

Younger patients and those with early stage lymphedema and
lower levels of disability at enrollment also perceived less disability
after participation in the lymphedema management program. The
findings suggest that early exposure to lymphedema management
may substantially decrease perceived disability among patients in
the early stages of lymphedema. As community-based lymphede-
ma management programs expand, an emphasis on prompt
enrollment of patients with stage 1 or 2 lymphedema will be
particularly important. Increased community awareness of LF and
efforts to reduce stigma will likely be vital to the identification and
enrollment of early stage lymphedema patients.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>95% CI</th>
<th>Adjusted</th>
<th>95% CI</th>
</tr>
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<tr>
<td><strong>Age Quartile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;45 Years</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>45–57</td>
<td>2.62</td>
<td>(−1.29, 6.54)</td>
<td>1.37</td>
<td>(−1.89, 4.62)</td>
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<tr>
<td>&gt;57–69</td>
<td>2.92</td>
<td>(−0.98, 6.83)</td>
<td>2.20</td>
<td>(−1.35, 5.74)</td>
</tr>
<tr>
<td>&gt;70</td>
<td>10.89</td>
<td>(7.03, 14.76)</td>
<td>7.89</td>
<td>(4.04, 11.74)</td>
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<tr>
<td><strong>Female Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2.85</td>
<td>(−0.07, 5.76)</td>
<td>5.73</td>
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</tr>
<tr>
<td><strong>Higher than Primary Education</strong></td>
<td>−6.88</td>
<td>(−10.40, −3.35)</td>
<td>−1.25</td>
<td>(−4.47, 1.98)</td>
</tr>
<tr>
<td><strong>Work</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed or Retired</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Homemaker or Housekeeper</td>
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<td>(−7.86, −3.40)</td>
<td>−5.76</td>
<td>(−8.22, −3.29)</td>
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<tr>
<td>Work or Study</td>
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</tr>
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<td>Married</td>
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<td>−1.29</td>
<td>(−3.84, 1.25)</td>
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<tr>
<td><strong>Caste</strong></td>
<td></td>
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<td></td>
<td></td>
</tr>
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<td>General Caste</td>
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<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Other Backward</td>
<td>0.76</td>
<td>(−2.34, 3.86)</td>
<td>1.43</td>
<td>(−1.10, 3.97)</td>
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<tr>
<td>Scheduled Caste</td>
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<td>(−8.35, 3.12)</td>
<td>1.85</td>
<td>(−2.80, 6.50)</td>
</tr>
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<td>Scheduled Tribe</td>
<td>2.12</td>
<td>(−4.57, 8.82)</td>
<td>4.69</td>
<td>(−0.99, 10.37)</td>
</tr>
<tr>
<td><strong>Any Chronic Health Condition</strong></td>
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<td>(4.27, 10.08)</td>
<td>5.45</td>
<td>(2.98, 7.92)</td>
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<tr>
<td><strong>Stage of Most-Affected Leg</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early (Stage 1–2)</td>
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<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Moderate (Stage 3)</td>
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<td>(0.91, 4.57)</td>
<td>1.91</td>
<td>(0.12, 3.71)</td>
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<tr>
<td>Advanced (Stage 4–6)</td>
<td>11.66</td>
<td>(8.34, 14.97)</td>
<td>8.38</td>
<td>(4.97, 11.80)</td>
</tr>
<tr>
<td><strong>Bilateral Lymphedema</strong></td>
<td>3.50</td>
<td>(0.68, 6.32)</td>
<td>−0.40</td>
<td>(−2.84, 2.04)</td>
</tr>
<tr>
<td><strong>Washing with Soap</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Less than Daily</td>
<td>−3.01</td>
<td>(−6.68, 0.65)</td>
<td>−3.63</td>
<td>(−7.55, 0.29)</td>
</tr>
<tr>
<td>At least Daily</td>
<td>−2.76</td>
<td>(−6.52, 1.00)</td>
<td>−2.21</td>
<td>(−6.24, 1.82)</td>
</tr>
<tr>
<td><strong>Exercise</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Less than Daily</td>
<td>−2.38</td>
<td>(−4.89, 0.14)</td>
<td>−2.64</td>
<td>(−5.17, −0.10)</td>
</tr>
<tr>
<td>At least Daily</td>
<td>−0.47</td>
<td>(−1.99, 1.06)</td>
<td>0.44</td>
<td>(−1.11, 1.99)</td>
</tr>
<tr>
<td><strong>Elevation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Less than Daily</td>
<td>−1.35</td>
<td>(−6.09, 3.39)</td>
<td>−0.43</td>
<td>(−4.98, 4.12)</td>
</tr>
<tr>
<td>At least Daily</td>
<td>0.17</td>
<td>(−1.67, 2.01)</td>
<td>0.34</td>
<td>(−1.53, 2.21)</td>
</tr>
<tr>
<td><strong>Wear Shoes Outside</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Often</td>
<td>−0.75</td>
<td>(−2.60, 1.11)</td>
<td>0.44</td>
<td>(−1.37, 2.25)</td>
</tr>
<tr>
<td>All of the Time</td>
<td>−2.80</td>
<td>(−4.56, −1.05)</td>
<td>−0.10</td>
<td>(−1.81, 1.61)</td>
</tr>
<tr>
<td><strong>Cream Use</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Often</td>
<td>−0.69</td>
<td>(−3.23, 1.84)</td>
<td>−0.05</td>
<td>(−2.50, 2.40)</td>
</tr>
<tr>
<td>All of the Time</td>
<td>1.23</td>
<td>(−0.21, 2.66)</td>
<td>0.80</td>
<td>(−0.64, 2.25)</td>
</tr>
<tr>
<td><strong>Any Interdigital Lesions</strong></td>
<td>5.06</td>
<td>(3.30, 6.82)</td>
<td>2.68</td>
<td>(0.85, 4.52)</td>
</tr>
<tr>
<td><strong>ADL Episode in the Past 30 Days</strong></td>
<td>11.49</td>
<td>(9.98, 13.00)</td>
<td>10.63</td>
<td>(9.10, 12.16)</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>1 Month</td>
<td>−5.06</td>
<td>(−7.33, −2.79)</td>
<td>−4.64</td>
<td>(−8.00, −1.29)</td>
</tr>
</tbody>
</table>
After controlling for other predictors, reporting an ADL episode in the previous 30 days remained a significant predictor of increased disability. Prior research has demonstrated that the prevention of ADL episodes slows long-term lymphedema progression [24,25]; our data demonstrate that reducing the number of ADL episodes also decreases patients’ perceived level of disability. Our results suggest that lymphedema management techniques that assist in preventing ADL episodes can reduce patient disability as well as increase productivity and participation in society. While this study focuses on perceived disability as a surrogate for quality of life, it is interesting to note that the maximal reduction in perceived disability occurred between 2 and 6 months, a period reported by others as the time of maximum impact on ADL episodes [26]. A more detailed analysis of the effect of this lymphedema management program on ADL episodes is underway.

These reductions in disability can have significant economic impact for both the patients and their communities. At twenty-four months post-enrollment, patients in our study gained an average of 2.4 work days per month as the result of decreased perceived disability. If extrapolated to all 17,036 (Little KM, unpublished data) lymphedema patients in Khurda District, this translates into approximately 2,688 person-years of productive time gained over the course of the twenty-four month study period. These findings suggest that substantial economic gains for individuals, families, and communities would result from an increased emphasis on LF morbidity reduction, especially in high-prevalence areas. In India, where nearly 20 million individuals suffer from symptomatic LF infections [9], the economic benefits of lymphedema management programs in terms of work days saved would be considerable.

Although lymphedema management improved disability scores over time, advanced lymphedema, the presence of other chronic health conditions, and female gender remained strong predictors of worse perceived disability. Though patients with advanced lymphedema experienced the largest reduction in their perceived disability during the study, their composite disability scores

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate</td>
<td>95% CI</td>
</tr>
<tr>
<td>2 Months</td>
<td>-6.44</td>
<td>(-8.74, -4.14)</td>
</tr>
<tr>
<td>3 Months</td>
<td>-7.26</td>
<td>(-9.52, -5.00)</td>
</tr>
<tr>
<td>6 Months</td>
<td>-8.41</td>
<td>(-10.56, -6.25)</td>
</tr>
<tr>
<td>12 Months</td>
<td>-6.18</td>
<td>(-8.43, -3.92)</td>
</tr>
<tr>
<td>24 Months</td>
<td>-5.68</td>
<td>(-8.39, -2.98)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Perceived Health Status in the Past 30 Days</th>
<th>Unadjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very good</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Good</td>
<td>7.96</td>
<td>(4.83, 11.10)</td>
</tr>
<tr>
<td>Moderate</td>
<td>15.77</td>
<td>(12.55, 18.99)</td>
</tr>
<tr>
<td>Bad</td>
<td>28.68</td>
<td>(25.26, 32.10)</td>
</tr>
<tr>
<td>Very bad</td>
<td>38.85</td>
<td>(33.10, 44.61)</td>
</tr>
</tbody>
</table>

Figure 4. Reported days work lost. Self-report of the mean number of days of work lost due to lymphedema-related disability in the past 30 days. Error bars represent 95% confidence intervals around the mean. All times were significantly different from baseline (time 0).

doi:10.1371/journal.pntd.0002100.g004
remained higher than young or early stage patients for the entire follow-up period. While community-based lymphedema management programs may provide increased access to hygiene supplies and education, they are typically unable to offer patients with advanced lymphedema more expensive and intensive therapies such as bandaging, antibiotics, and a specialized referral infrastructure. Effective control of LF-related morbidity may require dual development of low-cost community interventions alongside more complex services for patients with advanced lymphedema and other chronic health conditions. Further research should explore the feasibility and effectiveness of these interventions in low-resource settings. Opportunities for collaboration with other chronic health programs including those focusing on diabetes, leprosy, and venous insufficiency, should also be explored. Finally, future work should focus on women’s health in relation to lymphedema in an effort to reduce the disability gender-gap observed in this study.

Limitations
This study had several limitations. First, survey results were based on patient recall and perceived disability during the previous 30 days and may be subject to recall bias. Patients enrolled in this study were included based on the presence of lymphedema in one or both legs. Because blood was not drawn to test for the presence of microfilaraemia or filarial antigenemia the lymphedema management program may have enrolled patients with non-filarial lymphedema. Nevertheless, it is important to note that lymphedema management programs are recommended for lymphedema resulting from all causes. Additionally, the study is limited by the lack of a comparable control group not receiving the community-based lymphedema management program, as it is considered inappropriate to withhold knowledge of lymphedema management techniques from patients with lymphedema.

In order to account for repeat measurements over time, we used a mixed effects model that incorporated time as a variable in both the univariate and multivariate analyses. Because compliance with foot care was dramatically increased at all assessments subsequent to baseline, our model likely underestimates the effect of compliance with foot care on overall disability score. Indeed, compliance with foot care becomes highly significant when time is taken out of the model (data not shown). Finally, there was an increase in most WHO DAS II domain scores at 12 months compared to 6 months. It is not unexpected to see fluctuations in perceived disability from chronic diseases; more frequent or longer monitoring would provide a better sense of whether the benefits we have observed will be sustained. Future research will address the relationship between ADL episodes and lymphedema progression in this cohort.

Conclusion
While the effects of lymphedema management on clinical disease, disability, and quality of life have been studied previously [6,7,14,22], this is one of the first evaluations of a community-based lymphedema management program with 24 month longitudinal follow-up. Our findings indicate that community-based lymphedema management programs can reduce patient perceived disability and reduce the number of work days lost due to lymphedema symptoms. Significantly, these effects were maintained for two years following program enrollment. These data emphasize the need for national lymphatic filariasis elimination programs to prioritize morbidity management and disability prevention programs to improve the lives of those suffering from lymphedema associated with lymphatic filariasis.

Supporting Information
Checklist S1 STROBE Checklist. (DOC)

Acknowledgments
We are grateful to the lymphedema patients of Khurda District, Bolangarh Block, without whom this work could not be accomplished. We gratefully acknowledge the assistance of the CASA staff in Bhubaneswar including Soumenra Dhir, Grace Rao, Rajdeep Puri, Saroj Behera, Kuber Behera, and the CASA staff in New Delhi including Mr. Aloke Michyari and Mr. Sushant Agrawal, CASA Director. We also thank Dr. David Addiss of Children Without Worms, Dr. Michael Deming and Anna Blackstock of CDC, and Ann Varghese, Erika Pearl, Dr. Sarla Chand, Paul Derstine and Rick Santos of IMA World Health. We also acknowledge the cooperation and support of the Orissa Ministry of Health and Family Welfare.

Author Contributions
Conceived and designed the experiments: EKD JR LMF. Performed the experiments: PJB KML KEM EKD AP JR LMF. Analyzed the data: PJB KML KEM LMF. Wrote the paper: PJB KML LMF.

References