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Significant decline in lymphatic filariasis associated with nationwide scale-up of insecticide-treated nets in Zambia

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ABSTRACT

Lymphatic filariasis (LF) is a mosquito-borne disease, broadly endemic in Zambia, and is targeted for elimination by mass drug administration (MDA) of albendazole and diethylcarbamazine citrate (DEC) to at-risk populations. Anopheline mosquitoes are primary vectors of LF in Africa, and it is possible that the significant scale-up of malaria vector control over the past decade may have also impacted LF transmission, and contributed to a decrease in prevalence in Zambia. We therefore aimed to examine the putative association between decreasing LF prevalence and increasing coverage of insecticide-treated mosquito nets (ITNs) for malaria vector control, by comparing LF mapping data collected between 2003–2005 and 2009–2011 to LF sentinel site prevalence data collected between 2012 and 2014, before any anti-LF MDA was started. The coverage of ITNs for malaria was quantified and compared for each site in relation to the dynamics of LF. We found a significant decrease in LF prevalence from the years 2003–2005 (11.5% CI_{95} 6.6; 16.4) to 2012–2014 (0.6% CI_{95} 0.03; 1.1); at the same time, there was a significant scale-up of ITNs across the country from 0.2% (CI_{95} 0.0; 0.3) to 76.1% (CI_{95} 71.4; 80.7) respectively. The creation and comparison of two linear models demonstrated that the geographical and temporal variation in ITN coverage was a better predictor of LF prevalence than year alone. Whilst a causal relationship between LF prevalence and ITN coverage cannot be proved, we propose that the scale-up of ITNs has helped to control *Anopheles* mosquito populations, which have in turn impacted on LF transmission significantly before the scale-up of MDA. This putative synergy with vector control has helped to put Zambia on track to meet national and global goals of LF elimination by 2020.

1. Introduction

Lymphatic filariasis (LF) is a mosquito-borne disease, which is widely endemic in Zambia. Overall prevalence rates were estimated at 7.4% in 2011 from > 10,000 sampled individuals across 108 sites in all regions of the country by rapid circulating filarial antigen (CFA; a marker of the *Wuchereria bancrofti* adult worm infection) BinaxNOW Filariasis immunochromatographic test (ICT) card (Mwase et al., 2014). The initial mapping started in 2003 and 2005 at 42 sites across 14 districts thought to be endemic for LF.

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The prevalence ranged from 0% to 53.9% with the highest found in Lusaka and Western Provinces. Mapping in the remaining 58 districts was conducted at 65 sites in 2009 and 2010, with one site in early 2011. The prevalence ranged from 0% to 20.8% with the highest found in Luapula and Southern Provinces. This endemicity data helped the National LF Programme plan its elimination strategy with an estimated 11 million people requiring treatment. However, the scale-up of programmatic activities was slow to start in Zambia, as unlike many countries in Africa, it did not benefit from the African Programme for Onchocerciasis Control (APOC) that distributed free ivermectin to countries through the established and well trained community drug distributor (CDD) networks (World Health Organization (WHO), 2011).

The Global Programme to Eliminate Lymphatic Filariasis (GPELF) aims to eliminate LF by 2020 by interrupting LF transmission through mass drug administration (MDA) and controlling morbidity (WHO, 2010). In Zambia, as onchocerciasis is not endemic, the use of the drug combination of diethylcarbamazine citrate (DEC) and albendazole for MDA activities is recommended. Albendazole has long been donated to all country LF Programmes from GlaxoSmithKline (GSK), however, DEC had only recently become available for Zambia as a donated drug by Eisai Co., Ltd. (WHO, 2016a). In 2012 and 2014, Zambia conducted a national baseline sentinel site survey across 40 selected sites prior to the start of implementation activities so that impact could be measured over time. In 2015, Zambia successfully scaled up MDA to reach full geographical coverage with very high population compliance rates as part of its strategy to interrupt transmission, making it the largest and most successful distribution of DEC for LF in Africa in history (WHO, 2016a, 2016b).

LF is transmitted by certain anopheline species and the precise incrimination of those species in Zambia associated with transmission is limited. However, in many regions in Africa the LF *Anopheles* vectors are the same, or similar, to those of malaria, which are found across all regions of Zambia at varying distributions and species compositions (Wiebe et al., 2017; Coleman et al., 2017). For example, *Anopheles funestus* and *An. gambiae* are the predominant species in the wetter Eastern, Luapula, Northern and Lusaka provinces while *An. arabiensis* is more dominant in the drier southern region (Masaninga et al., 2013; Chanda et al., 2011; Kamuliwo et al., 2013). A study conducted in Luangwa district in 2011, associated *An. funestus* and *An. gambiae* with LF transmission, however, transmission was not directly confirmed (Shawa et al., 2013). Overall LF prevalence was found to be low (8.6%) and indicated a marked decline from prevalence measured in 2003 (33.3%) (Mwase et al., 2014), which the authors attribute to the concurrent scale up of vector control in the area.

Zambia's achievements in scaling-up interventions are distinctive as it has made tremendous strides over the past decade with very high coverage of vector control for malaria (Chanda et al., 2013). In line with the global trends to improve efforts in malaria control Zambia has put in measures to mitigate malaria transmission including vector control using insecticide-treated mosquito nets (ITN) (Chanda et al., 2012), which are distributed at antenatal and child clinics, equity programme and community mass distributions had reached over 60% at household level in 2008 with the aim of attaining 100% coverage (Chanda et al., 2011). Between 2010 and 2012 over 7 million new long-lasting insecticidal nets (LLINs) were delivered with up to 94% of the population potentially protected from malaria infection. The 2013–2014 Demographic and Health Survey (DHS) reported that around seven in 10 households (68%) owned an ITN, with Southern (79.5%), Eastern (77.1%) and Western (76.5%) Provinces reporting the highest provincial ITN coverage.

The aim of this study was to examine the putative association between LF prevalence and the nationwide scale up of ITNs; specifically, it compared the changes in LF prevalence between the prevalence mapping conducted between 2003 and 2011 and the baseline sentinel site mapping conducted prior to MDA in 2012 and 2014, and the coverage rates of ITNs during the corresponding periods.

2. Methods

2.1. LF prevalence patterns from 2003 to 2014

Endemicity mapping 2003–2011: Initial information on the geographical distribution of LF was based on two phases of mapping surveys conducted across Zambia by the Ministry of Health (MoH) Lymphatic Filariasis Control Programme (2003–2005) and the Programme for Integrated Control of Neglected Tropical Diseases (2009–2011). Community prevalence information was based on data collected from 10,193 individuals from 108 survey sites (Mwase et al., 2014), with the majority of data collected between 2003 and 2010, and only one site in early 2011. These surveys were conducted in accordance with the standard guidelines from the World Health Organization (WHO, 2000), which included adult individuals ($>$ 15 years of age) tested for the presence of CFA from finger-prick blood using the rapid BinaxNOW ICT card. The ICT card was read after 10 min as per manufacture instructions to avoid the possibility of false-positives if the tests are read too late. Details of the survey, methodology and locations have been described previously (Mwase et al., 2014).

Baseline sentinel site surveys 2012–2014: Prior to the implementation of MDA for the elimination of LF, baseline sentinel site surveys were conducted across the country in 2012 and 2014. The activity was part of standard routine monitoring and evaluation activities recommended by GPELF in order to measure impact and success of the National LF Programme over time (WHO, 2011). In total, 40 sites from the original LF surveys were selected based on the geographical distribution of the highest prevalence rates. The first four sentinel sites were surveyed in the Western Province of Zambia in 2012, and the remaining 36 sentinel sites were surveyed in 2014.

At each of the 40 sites between 200 and 300 participants aged $>$ 5 years were recruited and tested for the presence of CFA using the ICT card. For individuals testing ICT positive, a follow-up night blood test was conducted in order to detect the presence of *W. bancrofti* microfilaria (Mf), a marker of current infection, only detectable in the peripheral blood at night. The counting chamber