needed to achieve the 2020 elimination goal worldwide. Mathematical modelling suggested that the required duration of interventions can be halved by switching from annual treatment to 6-monthly treatment. This needs confirmation by empirical data. We aim to refine model-based estimates of the required duration of annual versus semi-annual MDA for achieving LF elimination, by analyzing DOLF project data. These include a community intervention study in Sikka district, Flores, Indonesia that compared trends in brugian and bancroftian filariasis infection in 3 communities after 3 years of annual or biannual MDA with diethylcarbamazine and albendazole. We fitted the LYMFASIM simulation model to antigenaemia prevalence (*W. bancrofti*), antibody prevalence (*B. timori*), and microfilaraemia (mf) prevalence and intensity (both species) at baseline. Thereafter we assessed whether the model-predicted trends are in accordance with the observed data. Lastly we estimated the number of treatment rounds required to bring mf prevalence below 1%. The baseline prevalence in the community with biannual MDA was higher (8.7 and 10.3% for *W. bancrofti* and *B. timori*, respectively) than for the two communities with annual MDA (0 and 0.4% for *W. bancrofti* and 3.9 and 4.9% for *B. timori)*. Our modeling approach accurately reproduced the observed trends. Because of the low baseline mf prevalence in the communities with annual MDA, these communities reached the 1% pre-TAS threshold faster than the community with annual MDA. Our modelling suggests that the target would have been achieved later than in the biannual village, if the baseline mf prevalence was equally high. The total required duration of MDA can be about halved by treating biannually instead of yearly, for both LF species, provided that good coverage levels are maintained. This is a useful strategy to accelerate MDA where biannual MDA can be implemented.

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A COMPREHENSIVE ASSESSMENT OF PERSISTENT *WUCHERERIA BANCROFTI* IN HOTSPOTS IN GALLE COASTAL EVALUATION UNIT IN SRI LANKA 9 YEARS AFTER STOPPING MASS DRUG ADMINISTRATION

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The Sri Lankan Anti-Filariasis Campaign (AFC) distributed 5 rounds of MDA (DEC plus ALB) according to WHO guidelines to some 10 million people in 8 endemic districts between 2002 and 2006. All districts met WHO criteria for verification of lymphatic filariasis (LF) elimination as a public health problem in 2016. We previously reported results from comprehensive post-MDA surveillance that was conducted in Galle district between 2013 and 2014. These results and a district wide molecular xenominitoring study suggested that there were many hotspots in coastal EU in Galle district with ongoing transmission. One of these hot spots called Balapitiya PHI (Population: 17,500) had alarmingly high LF parameters: community CFA rate (3%, 1.8-4.8 CI), MF rate (1%, 0.4-2.2% CI); school children CFA rate (1.2%, 0.5-2.8% CI), Bm14 antibody rate (5.7%, 3.7-8.4% CI) and filarial DNA rate in *Culex* (5.2%, 4.2-6.3% CI). Microfilaremia rates in this area ranged from 0.9% in 2013 and 0.6% in 2016 suggesting that 2 rounds of MDA in 2014 and 2015 may have had some effect. We reexamined 22 of 168 PHM areas in the Galle district coastal EU after 2 rounds of MDA, and 8 of these were drawn from Balapitiya. Approximately 660 *Culex* pools collected from 22 PHMs in Galle were tested for filarial DNA. 179/660 (27%) pools were positive for filarial DNA. Interestingly, a higher percentage of mosquito pools [107/240 pools (45%)] sampled from Balapitiya contained filarial DNA. This hotspot may require additional rounds of MDA with improved coverage or a test and treat program along with integrated vector management. Coastal Galle district and Balapitiya provide excellent opportunities for applied field research to compare different methods for erasing hotspots and for strengthening Transmission Assessment Surveys.

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HYPO-ENDEMIC ONCHOCERCIASIS HOTSPOTS: CHARACTERIZING RISK, DEMOGRAPHY, INFRASTRUCTURE AND ENVIRONMENT TO FACILITATE THE SCALE UP OF ALTERNATIVE STRATEGIES FOR ELIMINATION IN CENTRAL AFRICA

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Community directed treatment with ivermectin (CDTi) has been successful in reducing and controlling the global prevalence of onchocerciasis, with elimination now targeted in all endemic countries. However, in Africa, severe adverse events (SAEs) from ivermectin treatment, including death, have been reported in some areas that are hyper-endemic for loiasis. We define 'hypo-endemic onchocerciasis hotspots' as areas of overlapping onchocerciasis hypo-endemicity and loiasis hyper-endemicity. In such hotspots, the potential risks of CDTi may outweigh the benefits to individual patients, and if left untreated, could contribute to on-going transmission and prevent meeting elimination targets for onchocerciasis. Alternative intervention strategies such as anti-*Wolbachia* therapy, vector control and/or the Test and (not) Treat need to be implemented in such hotspots to ensure safety and impact. It is important however to first understand the local risk, demography, infrastructure and environment that characterise the hotspots. This study, therefore, aimed to characterise five hypo-endemic hotspots across central Africa. Firstly, by using onchocerciasis and loiasis prevalence data to define the scale and spatial extent of risk; secondly, by examining key demographic factors including: age, sex, population density and distribution; thirdly, infrastructure factors including: health facilities, roads and nearest large town, and finally, environmental factors, including: rivers, forests and elevation. These key characteristics were summarised, mapped with key information and used to develop a simple algorithm/decision matrix to facilitate country programmes in identifying high-risk areas, target populations, available human resources, access to health infrastructure and logistical requirements to successfully implement alternative interventions. This study considers whether this pragmatic approach can bridge an existing gap between academic research and programme implementation in hypo-endemic hotspots, in countries currently falling behind in the WHO onchocerciasis elimination agenda.

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MEASURING THE NUMBER OF REPRODUCTIVE ADULT FEMALES AND DEFINING TRANSMISSION ZONES FOR FILARIAL NEMATODES USING POPULATION GENETIC MEASURES

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For most organisms, there are limits to the distance over which mating can occur between any two individuals, giving rise to population structure in which genetic relatedness is correlated with distance: close together, more related (i.e. more likely to share common ancestors) and further

apart, less related. The result is that measures of genetic relatedness can be used to assign an individual to their population of origin, and that measures of population structure can define the boundaries within which mating between two individuals is likely to occur. For filarial nematodes, two individuals can only mate if they are transmitted to the same host, so measures of genetic relatedness in filarial parasites are an indirect measure of the distances over which transmission occurs within a given population. Consequently, measures of population structure define the boundary of a parasite transmission zone and estimate the probability that an individual parasite is a "resident" of that transmission zone or is an immigrant. Similarly, measures of population structure can be used to estimate the risk of parasite transmission between two locations (for example, across a border between countries/states/districts with differing degrees of success in parasite elimination). We have used a variety of genotyping tools (whole genome sequencing, whole and partial mitochondrial and *Wolbachia* sequencing, and single locus genotyping) to characterise population structure and hence transmission zones for *Onchocerca volvulus* in West Africa and have shown that we can resolve population structure and transmission zones over several spatial and temporal scales. These measures may provide objective tools with which to determine the boundaries of implementation and evaluation units for mass drug administration and cessation of treatment. We have also coincidentally used genotyping data to estimate the number of females contributing to the microfilarial population in the skin of an individual patient, providing a novel measure of parasite infection intensity, and to track the rate at which a parasite population declines under MDA.

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DEVELOPING THE FIRST NATIONAL DATABASE AND MAP OF LYMPHATIC FILARIASIS CLINICAL CASES IN MALAWI

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The Lymphatic Filariasis (LF) Elimination Programme in Malawi is on track to meet the Global Programme to Eliminate Lymphatic Filariasis (GPELF) targets of 2020 by interrupting transmission with mass drug administration (MDA) and alleviating suffering by managing morbidity and preventing disability (MMDP). This study aimed to highlight the LF programme's approach to determining the number of people affected by lymphoedema and hydrocoele, and developing the first national database and morbidity map for targeted interventions across the 26 endemic districts. Such information is essential for certification of LF elimination as a public health problem. The first data on morbidity was collected during national MDA campaigns in 2009-2010 when community drug distributors (CDDs) reported the number of lymphoedema and hydrocoele cases at the health-centre-level. Once MDA was stopped in 2014, the three districts with the highest baseline prevalence and reported number of cases during MDA (Chikwawa, Nsanje and Karonga), were selected for intensive patient mapping using the mHealth tool *MeasureSMS-Morbidity* in which health surveillance assistants (HSAs) reported all cases in their communities by SMS. Each district reported approximately 350 lymphoedema and 800 hydrocoele cases, and provided specific village-level patient data on age, sex, condition and severity of condition (mild, moderate, severe) which could be used to further understand spatial-epidemiological patterns. Focal mapping is now planned for six to eight districts to help develop predictive maps in the remaining 23 districts. Each district will be strategically selected, considering its location, environment, baseline prevalence, and morbidity data reported by MDA. This will allow country-wide data and a map to be generated, highlighting and classifying areas of 'low', 'medium' and 'high' predicted prevalence/case numbers, which will then be verified. This information will allow the Malawi LF Programme to appropriately plan and deliver a basic package of care to those suffering from the disabling and debilitating clinical manifestations of LF across the country.

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FAMILIAL AGGREGATION AND HERITABILITY OF *LOA LOA* INFECTION

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Large scale treatment with ivermectin (IVM) against onchocerciasis needs to be expended to hypo-endemic areas to reach the elimination goal. In these areas, localities where community-directed treatment with IVM (CDTI) cannot be applied because of possible occurrence of *Loa*-related severe adverse events (SAE) have to be identified. At individual level, people at risk of SAE are those harboring >30,000 *Loa* microfilariae per mL of blood. For a given prevalence of microfilaremia, the proportion of people with such high densities varies significantly between communities. We hypothesized that the latter observation is related to the existence of familial clusters of hypermicrofilaremic individuals which would be the consequence of a genetic predisposition to present high *Loa* microfilarial densities. We tested this hypothesis in 10 villages in the Okola Health District of Cameroon. Intrafamilial correlation coefficients and heritability estimates were assessed for both *Loa* microfilaremia and individual microfilarial densities by controlling for age, sex, *Mansonella perstans* microfilaremia and household effects. Pedigree charts were constructed for 1,126 individuals. A significant familial susceptibility to be microfilaremic for *Loa* was found for first-degree relatives ($\rho = 0.08$, $P < 0.05$; heritability = 0.23). Regarding individual microfilarial densities, a significant familial aggregation was demonstrated ($\rho = 0.36$ for first- and 0.27 for second-degree relatives). For first-degree relatives, the highest coefficients were found between mothers and daughters ($\rho = 0.57$). Overall heritability estimate for intensity was 0.24. These results suggest that the *Loa* microfilaremic status is mainly driven by environmental factors and habits, while a genetic component governs the microfilarial density. These results support the hypothesis that a genetical predisposition to be hypermicrofilaremic exists, leading to the presence of familial clusters of individuals at risk for post-ivermectin SAE. This finding should be taken into account for developing sampling strategies to identify communities where CDTI cannot be applied.

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PREDICTIVE VALUE OF OV16 ANTIBODY PREVALENCE IN DIFFERENT AGE GROUPS FOR ELIMINATION OF AFRICAN ONCHOCERCIASIS

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Onchocerciasis is targeted for elimination in Africa by 2025 through mass drug administration (MDA) with ivermectin. Current WHO guidelines for stopping MDA and verifying elimination require that the Ov16 antibody prevalence in 0-9 year old children is brought below 0·1%, but the empirical evidence underlying the choice of age group and threshold is still limited. We assessed the predictive value of different Ov16 antibody prevalence thresholds for elimination of onchocerciasis, for various age groups, a variety of endemic settings and various MDA scenarios. We used the individual-based stochastic ONCHOSIM model to simulate trends in infection and Ov16 antibody prevalence levels during and after MDA. We