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## LYMPHATIC FILARIASIS RESIDUAL TRANSMISSION HOTSPOTS IN AMERICAN SAMOA

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To achieve elimination of lymphatic filariasis, American Samoa carried out 7 rounds of mass drug administration from 2000 to 2006 and passed Transmission Assessment Surveys (TAS) in 6-7 yr-old children in 2011 and 2015, although 1 or 2 ICT-positive children were found on each occasion in the same school. Serology studies using Og4C3, Wb123 and Bm14 in 807 adults in 2010 identified higher antigen prevalence in two spatial clusters, one of which included the school attended by ICT-positive children in both TAS. Prevalence was higher in men and those residing in American Samoa for <5 yrs. To follow up these findings, a targeted study in 2014 tested three groups of individuals: 124 residents aged 3-70 yrs in the two putative 'hotspots'; 337 children aged 7-13 yrs in the school where ICT-positives had been identified in TAS; and 650 adult workers (residing across the island) attending a pre-employment clinic or working in the tuna cannery. Overall prevalence (N=898 to 1,111 depending on the test) was 2.1% (95% CI 1.3-3.1%) for ICT and Og4C3, 5.7% (4.2-7.3%) for Wb123, and 10.2% (8.5-12.2%) for Bm14. The study confirmed elevated prevalence of ICT and Og4C3 (both 8.1%) antigen as well as Wb123 (9.8%) and Bm14 (23.6%) antibody in all ages in the two suspected hotspots. Bm14 antibody prevalence was higher in males than females in all groups (32.1% vs 17.1% in hotspot villages (p=0.05); 19.9% vs 7.0% in adult workers (p<0.001); and 3.3% vs 0.6% in children aged 7-13 yrs (p=0.06)). All ICT positive persons were treated and had slides taken. Microfilariae (Mf) with density from 8 to 3267/ml were observed on 4 of 20 slides examined, with all Mf positive persons residing in hotspots. Thus age, gender and residence in a hotspot village were the predominant risk factors for being positive for diagnostic markers of LF. This study has confirmed the suspected hotspots previously identified in 2010 from a spatially representative adult sample as sites of continuing transmission and potential sources of resurgence. The results further support the potential use of spatial epidemiological methods for identifying residual foci of infection in the endgame phase of LF elimination programs.

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## EXCESS MORTALITY ASSOCIATED WITH HIGH LOA LOA MICROFILAREMIA IN THE EAST REGION OF CAMEROON: A RETROSPECTIVE COHORT STUDY

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Loiasis affects more than 10 million people, most in Central Africa. Besides its classical signs ("eye worm" and "Calabar swelling"), it has also been reported as a cause of renal and cardiac complications. However, the burden of loiasis has never been assessed and it is still considered a benign condition. To assess whether loiasis bears any excess mortality, we conducted a retrospective cohort study in the East Region of Cameroon. In 2001, 3,627 individuals living in 28 villages were included in a survey during which thick blood smears (50 µL) were analyzed for *Loa loa* microfilarial (mf) density. In 2016, these villages (where no mass ivermectin treatment has ever been organized) were visited again to assess whether the subjects examined 15 years before were still alive. The vital status could be determined for 3,301 individuals (91%). Data analyses included (a) an analysis at the community level between the age- and

sex-standardized prevalence of (hyper)-microfilaremia in 2001 and the standardized mortality rates (SMR); (b) an assessment, using multivariate accelerated failure model, of the excess mortality relative to the initial mf density (4 classes: 0, 1-8,000, 8,000-30,000 and >30,000 mf/mL); (c) the calculation of the population-attributable fraction of mortality due to presence (vs. absence) of a *Loa* microfilaremia. At community level, the SMRs increased by 5.5% when the proportion of subjects with >30,000 mf/ml increased by 1% (P=0.040). A similar trend was observed when the threshold was 8,000 mf/ml (2.9%/1%; P=0.068). People aged >25 years with more than 30,000 mf/mL in 2001 died significantly earlier than those with lower mf densities (Time Ratio=0.67, 95% CI: 0.48-0.95, P=0.024). Lastly, 14.5% (95% CI: 6.5-21.8) of all-cause mortality was attributable to the presence of *Loa* mf. In conclusion, high *Loa* microfilaremia was associated with increased mortality in the study site. There is a need to validate our observations in other *Loa* areas, as they are likely to have implications on the status of loiasis in terms of public health, and the implementation of onchocerciasis and lymphatic filariasis elimination programs in Central Africa.

## 3

## PROGRESS TOWARDS ONCHOCERCIASIS ELIMINATION IN THE PARTICIPATING COUNTRIES OF THE AFRICAN PROGRAM FOR ONCHOCERCIASIS CONTROL: EPIDEMIOLOGICAL EVALUATION RESULTS

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The African Programme for Onchocerciasis Control (APOC) was created in 1995 in order to control onchocerciasis as a public health problem by implementing sustainable Community Directed Treatment with Ivermectin (CDTI). When research showed that mass treatment can lead to complete elimination of the infection in Africa, APOC shifted its target to elimination of infection and interruption of transmission. Epidemiological evaluations have been undertaken from 2008 to 2014 in evaluation areas with ≥6 years of effective treatment. We analyzed these unique data, to assess progress towards elimination. Epidemiological evaluations were done per area, in two phases. First, parasitological surveys were done in about 10 selected high risk communities per area with high pre-control endemicity level. By comparing observed prevalence levels to expected trends (as predicted by the established ONCHOSIM model, developed at Erasmus MC Rotterdam, and extensively used for policy support in onchocerciasis control in Africa), using Bayesian methods and Monte Carlo simulation, we classified the progress towards elimination as "faster than predicted", "on track", or "delayed". Second, in areas close to elimination, additional parasitological surveys were done in more communities to assess whether mass ivermectin treatment can safely be stopped. Initial parasitological surveys covered 54 areas, 639 villages and 127,665 people out of 53 million total population. The decline in prevalence was faster than predicted in 23 areas, on track in another 23 and delayed in 8 areas. Additional surveys were done in 22 areas and 13 of these met the epidemiological criteria for stopping treatment. Overall, 32 areas (25.4 million people) had reached or were close to elimination, 18 areas (17.4 million) were on track but required more years treatment, and in 8 areas (10.4 million) progress was unsatisfactory. Great progress has been made by APOC in realizing elimination beyond its prime goal. Elimination is reached or close for millions of people. Extra effort is needed in areas with unsatisfactory progress.