PhD defence Joseph Okebe

From control to elimination: reducing residual malaria transmission in The Gambia.

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Dit is de omschrijving

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Summary:

Malaria endemic countries such as The Gambia, backed by political will and international funding, have significantly reduced the malaria burden. This has renewed interest in malaria elimination, which is extraordinary given that the previous attempt at eradication in the '50s did not achieve its intended target and, more importantly, excluded sub-Saharan Africa. The situation creates opportunities for learning to understand current trends in transmission and evaluate strategies that would enable countries achieve malaria elimination.

Areas where malaria has been eliminated or elimination is being studied have unique ecological features such as their location (islands) or weather conditions that may be encouraging for malaria elimination. These profiles do not reflect most endemic countries, especially in sub-Saharan Africa, however the significant reductions in these previously high transmission areas indicate that elimination may be feasible but with a different approach. One of such is the concept of progressively shrinking the area where transmission occurs. It has been observed that countries with the largest reductions in transmission had lower baseline endemicity and many of these were at the fringe of the "malaria map". Thus, countries such as The Gambia, which has made substantial reductions in malaria-related morbidity and mortality provide platforms for such research. Compared to estimates in 2000, the country has reduced case incidence and malaria admissions by 75% and >50% respectively with >50% of the population at risk having access to an insecticide-treated mosquito net. The interventions for control include laboratory testing of suspected cases and treatment with an artemisinin-based combination therapy (ACT), spraying walls of living areas with residual insecticides, sleeping under insecticide-treated bed nets, preventive treatment of pregnant women and children less than 5 years (during the short transmission season).

However, the disease burden has not declined at the same rate, which suggests underlying heterogeneity in transmission across the country, and has important implications for planning elimination.

In the first stage of this project, we investigated this heterogeneity through a nationwide cross–sectional survey of primary school children >5 years of age to determine parasite and serological prevalence. The choice of parasitological and serological indicators are to identify short and medium-term changes in transmission. The results confirmed the reduction in parasite carriage and exposure compared to earlier reports but also relatively higher parasite and serological prevalence towards the east of the country.

The findings of the study were also consistent with the growing evidence on the potential role of asymptomatic parasite carriage and foci of transmission. Treating asymptomatic carriers in these locations could further reduce transmission and the World Health Organisation recommends the use of primaquine with an ACT for *Plasmodium falciparum* endemic areas considering elimination. Critics of this recommendation cited the weak evidence supporting the recommended dose primaquine and its poor safety record. Primaquine was initially developed against *P. falciparum* but was abandoned because of the risk of a dose-related haemolytic anaemia especially in people deficient in the glucose-6-phosphate dehydrogenase (G6PD); an enzyme that help protect red blood cells against damage by agents such as primaquine. Because the distribution of this deficiency is correlated to malaria, defining the prevalence of deficiency can help inform decisions on primaquine's use.

In the second study, we evaluated the prevalence of G6PD deficiency and showed low prevalence of genotype and phenotypes of deficiency in the country and, a weal association between both profiles.

The next study in the project was a randomized controlled trial to determine the primaquine dose that maximises efficacy and safety by comparing the erstwhile-recommended dose against lower doses in asymptomatic malaria-infected G6PD-normal individuals. The results showed that primaquine, at doses as low as 0.20mg/kg, substantially reduced gametocyte carriage and that although the risk was low, post-treatment transmission with ACTs or combined with primaquine at 0.20mg/kg dose may occur despite reductions in gametocyte carriage. None of the participants who received primaquine has clinically significant effects despite reductions in haemoglobin counts and these recovered to baseline values. This study was not designed to address the risks in G6PD but provides the basis for testing lower doses in this high-risk population.

The findings of the project contribute to the growing evidence on the nature of changing transmission ways to further reduce and eventually interrupt transmission. Potential next steps would be to see how and where these can be operationalized as part of a programme for malaria elimination such as mass or targeted drug treatment. This must be supported with improved surveillance to track on-going changes in transmission trend as well as impact of new tools such as primaquine