**THE IMPACT OF TRANSMISSION REDUCTION ON THE EVOLUTION OF *P. FALCIPARUM* DRUG RESISTANCE.**

**Data Description:**

Data for this project comes from antimalaria drug resistance marker surveillance studies conducted by various research groups across endemic regions of the world. These include countries in Africa, Asia, Oceania, Central, South America and the Caribbean with different transmission intensities. Here mutations in the *Plasmodium falciparum* genes such as the *pfcrt* and *pfmdr1* (associated with Chloroquine, Mefloquine and ACT resistance); *pfdhps* and *pfdhfr* (associated with resistance to Sulphadoxine Pyrimethamine) were tracked and quantidied. These data spanning a period from 1995 to 2022 were then stored in a database run by the WorldWide Antimalarial Resistance Network (WWARN). WWARN is a global collaboration of infectious disease experts for the generation, analysis and application of malaria drug resistance data.

Briefly for these studies, individuals from various age groups were screened using mainly Microscopy and Rapid Diagnostic Tests for the presence of the malaria parasite *Plasmodium falciparum.* Capillary blood was then taken from those that tested positive and this was followed by parasite DNA isolation. Following this, the parasites were genotyped for the various antimalaria drug resistance genes, including the *pfcrt*, *pfmdr1*, *pfdhps* and *pfdhfr* genes and their mutations quantified and analysed.

My proposed project seeks to gain insights on the relationship between transmission intensity changes as measured by prevalence of parasitemia (parasite rate) and the spread of drug resistance over time. This is because the emergence and spread of drug resistant *P. falciparum* threatens to foil the progress made with control interventions. One of the main methods for assessing drug efficacy and resistance apart from clinical drug efficacy assessment and ex vivo/invitro drug sensitivity methods is the use of molecular markers. These serve as valuable tools as their frequency in a population of parasites is a good indicator of the level of clinical resistance (Menard & Dondorp, 2017). Understanding how transmission intensity changes impact on the evolution of drug resistance is vital to the control of the disease. This will have implications on whether transmission-reducing malaria control efforts will have additional benefits or not. The drug resistance data is going to come from the WWARN database while the parasite rate data will come from the Malaria Atlas Project Database (MAP). Like WWARN, this repository aims to disseminate free, accurate and up-to-date information on malaria and associated topics. This includes prevalence and incidence distribution, as well as the distribution of antimalarial drugs, insecticide treated nets, mosquito vectors, and human blood disorders.

**Aims of the experiments**:

The aims of this project include: 1. Report and compare frequency *of pfcrt, pfmdr1, pfdhps*, *pfdhfr* mutations and Parasite rate in endemic regions. 2. Explain the association of factors such as: year of study and parasite rate with the reported frequency of the mutations.

**Hypothesis:**

Low transmission intensity (parasite rate) exposes parasites to high inbreeding and low sexual recombination, and this increases the frequency of mutant genotypes. Similarly, high transmission intensity exposes parasites to high outcrossing and high sexual recombination and this decreases the frequency of mutant genotypes.

**Proposed methods:**

A general linear mixed model will be used to assess the association of factors such as: year of study and parasite rate on the reported frequency of mutations. In the model, study/ID will be the random effect whiles factors such as year of study and parasite rate will be as considered fixed effects. Figures to communicate my findings will include plots of the mutant frequencies (dependent variable) against year of study and parasite rate (independent variables). Also, ggplot in the tidyverse package will be used for plots, while lm in the lme4 package will be used for model analysis. P value < 0.05 will be considered to indicate statistical significance.

**Simple summary stats of the data:**

Chart, scatter chart

Description automatically generated

**References:**

Menard, D., & Dondorp, A. (2017). Antimalarial drug resistance: a threat to malaria elimination. Cold Spring Harbor Perspectives in Medicine, 7(7), a025619.