

## **Intensity of transmission and spread of gene mutations linked to chloroquine and sulphadoxine-pyrimethamine resistance in falciparum malaria.**

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Received 20 March 2003, Revised 27 May 2003, Accepted 4 June 2003, Available online 15 July 2003.

[https://doi.org/10.1016/S0020-7519\(03\)00156-5](https://doi.org/10.1016/S0020-7519(03)00156-5)

### **Abstract**

The number of malaria parasite clones per infection-multiplicity of parasite clones-is affected by the transmission intensity, multiplicity increases with increasing transmission. This affects the frequency of parasites' sexual recombination and, if several mutations in different genes are involved, can break down drug resistant genotypes. Therefore, the effects of malaria transmission intensity on the spread of drug resistance could vary depending on the number of genes involved. Here we show that, compared to low transmission, intermediate-high transmission is associated with a 20–100-fold lower risk for the mutations linked to chloroquine resistance and a 6–17 times higher risk for those linked to sulphadoxine-pyrimethamine resistance. This is consistent with the hypothesis of a mutagenic basis for chloroquine resistance and a monogenic basis for that of sulphadoxine-pyrimethamine. Reducing transmission intensity could slow the spread of resistance. However, a reduction below a critical threshold (e.g. when parasite prevalence in children 2–9 years old is around 60–80%) could, paradoxically, accelerate

the spread of resistance to chloroquine and possibly to other drug combinations whose basis is mutagenic. Our findings have important implications for malaria control because increasing drug resistance has a substantial impact on mortality.

### **Keywords**

Malaria transmission intensity; *Plasmodium falciparum*; Drug resistance; Gene mutation; Chloroquine; Sulphadoxine-pyrimethamine