

## **Publication**

Age-shifting in malaria incidence as a result of induced immunological deficit: a simulation study

## JournalArticle (Originalarbeit in einer wissenschaftlichen Zeitschrift)

**ID** 3180888

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Year 2015

**Title** Age-shifting in malaria incidence as a result of induced immunological deficit: a simulation study **Journal** Malaria journal

Volume 14

Pages / Article-Number 287

Keywords Malaria, Epidemiology, Vaccines, Chemoprevention, Age shift

Effective population-level interventions against Plasmodium falciparum malaria lead to age-shifts, delayed morbidity or rebounds in morbidity and mortality whenever they are deployed in ways that do not permanently interrupt transmission. When long-term intervention programmes target specific agegroups of human hosts, the age-specific morbidity rates ultimately adjust to new steady-states, but it is very difficult to study these rates and the temporal dynamics leading up to them empirically because the changes occur over very long time periods. This study investigates the age and magnitude of age- and time- shifting of incidence induced by either pre-erythrocytic vaccination (PEV) programmes or seasonal malaria chemo-prevention (SMC), using an ensemble of individual-based stochastic simulation models of P. falciparum dynamics. The models made various assumptions about immunity decay, transmission heterogeneity and were parameterized with data on both age-specific infection and disease incidence at different levels of exposure, on the durations of different stages of the parasite life-cycle and on human demography. Effects of transmission intensity, and of levels of access to malaria treatment were considered. While both PEV and SMC programmes are predicted to have overall strongly positive health effects, a shift of morbidity into older children is predicted to be induced by either programme if transmission levels remain static and not reduced by other interventions. Predicted shifting of burden continue into the second decade of the programme. Even if long-term surveillance is maintained it will be difficult to avoid mis-attribution of such long-term changes in age-specific morbidity patterns to other factors. Conversely, short-lived transient changes in incidence measured soon after introduction of a new intervention may give over-positive views of future impacts. Complementary intervention strategies could be designed to specifically protect those age-groups at risk from burden shift.

Publisher BioMed Central ISSN/ISBN 1475-2875

edoc-URL http://edoc.unibas.ch/dok/A6419752

Full Text on edoc Available;

Digital Object Identifier DOI 10.1186/s12936-015-0805-1 PubMed ID http://www.ncbi.nlm.nih.gov/pubmed/26206255

ISI-Number WOS:000358400600002

Document type (ISI) Journal Article