Understanding the impact of control interventions on Onchocerciasis-Associated Epilepsy using the EPIONCHO-IBM transmission model

Jacob Stapley*, Jonathan Hamley*, Martin Walker**, Samit Bhattacharyya*** & Maria-Gloria Basáñez*
Department of Infectious Disease Epidemiology, Imperial College London*. In collaboration with RVC** & Shiv Nadar University***

Background

- Onchocerciasis or “river blindness”, is a filariasis caused by *Onchocerca volvulus and* transmitted via bites of *Simulium* (Diptera) blackflies.
- Most clinical sequelae are caused by the microfilariae (the worms’ larval progeny).
- Suspected cause of epilepsy in endemic areas (Onchocerciasis Associated Epilepsy, OAE) but aetiological & epidemiological evidence remain inconclusive.
- Chesnais *et al.* (2018) were the first to link **mf load** during childhood (aged 5-10 years) to **OAE onset later in life** in a **dose-dependent manner.**
- EPIONCHO-Individual Based Model (IBM) is a stochastic age-and sex-structured model of onchocerciasis transmission (Hamley *et al*. 2019).

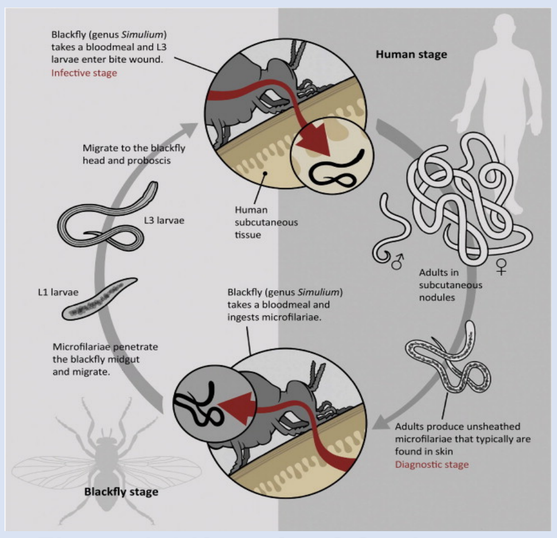

Figure 1. Lifecycle of *Onchocerca volvulus* (From Basáñez *et al.* 2006)

Aims

1. Parameterise EPIONCHO-IBM to capture baseline transmission conditions of Chesnais *et al.* (2018).
2. Incorporate OAE into EPIONCHO-IBM using an onset probability function.
3. Perform sensitivity analyses of OAE prevalence.
4. Model the effect of ivermectin Mass Drug Administration (MDA) on OAE dynamics.

Methods

Parameterisation

- Determine input parameters (Annual Biting Rate, ABR) to capture baseline conditions in Chesnais *et al.* (2018)

Probability Function

- Determine relationship between OAE onset probability and mf load in children aged 3-10 years

OAE Outputs

- Incorporate OAE into EPIONCHO-IBM using R software and determine OAE prevalence and incidence

Impact of Ivermectin

- Model 25 years of annual ivermectin MDA and obtain prevalence and incidence dynamics of OAE

Results

- An ABR (no. bites/person/year) of 41,922 was the minimum required to generate mean mf loads in the 5-10-year-old cohort of Chesnais *et al.*

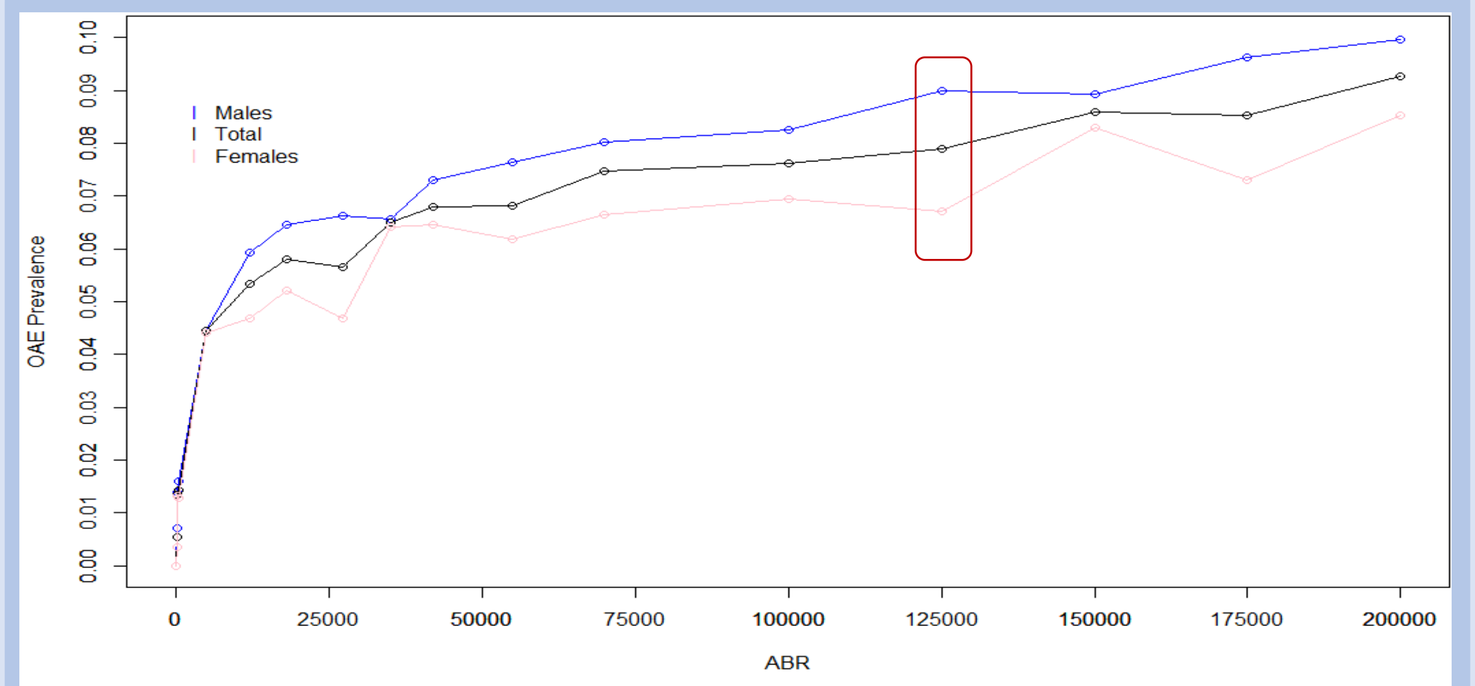

Figure 2. Sensitivity analysis of OAE prevalence to variation in ABR (for population aged 30-35 years only). OAE prevalence vs ABR was plotted for the age group 30-35 years using EPIONCHO-IBM to compare the OAE prevalence with that documented by Chesnais *et al.* in this age group 25 years after baseline study (8.2% in the total sample; 9.6% in males and 6.8% for females). The red open box indicates that these values are closely reproduced by EPIONCHO-IBM for an ABR of 125,000.

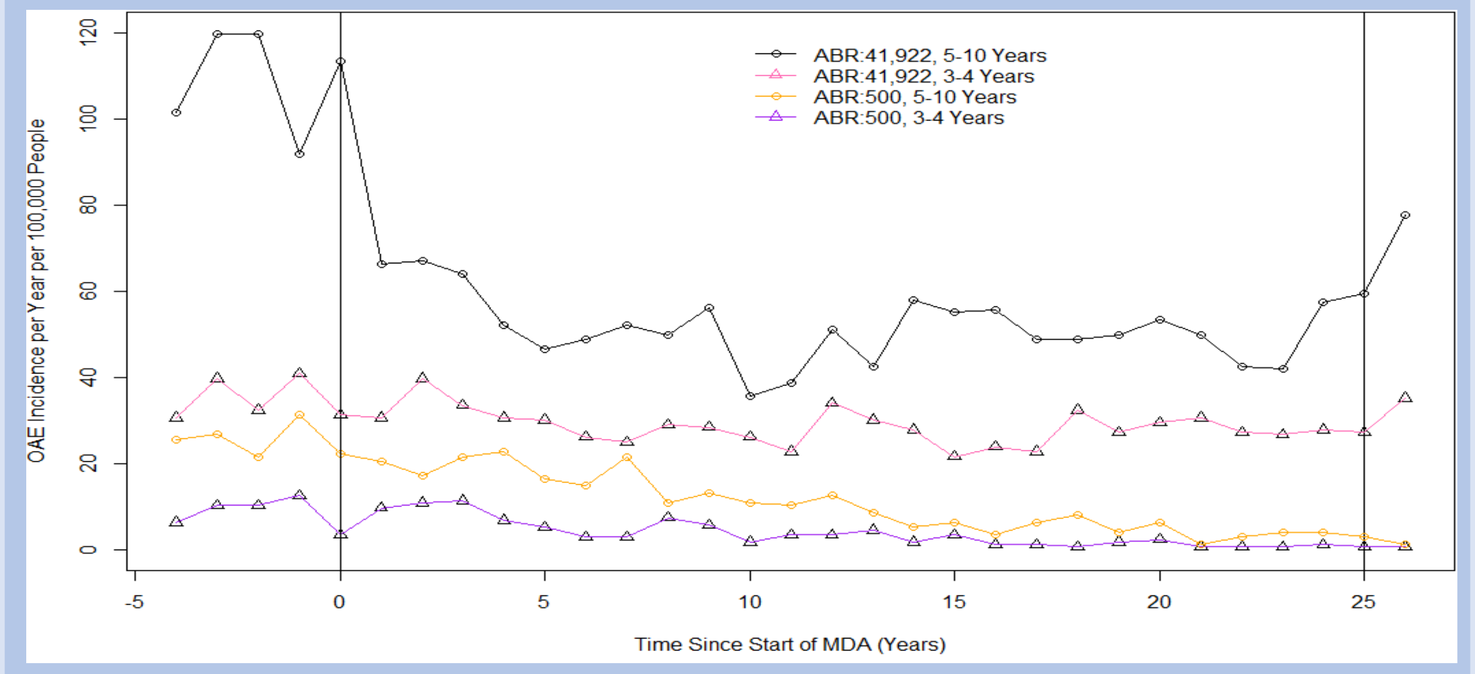

Figure 3. OAE incidence dynamics during 25 years of annual ivermectin MDA for 3-4-year-olds (untreated) and 5-10-year-olds (treated). Twenty-five years of annual ivermectin MDA were simulated with EPIONCHO-IBM for two ABR values and ‘standard’ coverage (65% of total population and 5% of systematic non-adherence). OAE incidence decreases in the treated group (those aged ≥5years) but does not change substantially in the untreated group, particularly for high ABR. For low ABR, annual ivermectin MDA leads to elimination of transmission and elimination of OAE, and therefore, the untreated group benefits from the interruption of transmission.

Conclusions & Future Work

- ✓ OAE was incorporated into EPIONCHO-IBM.
- ✓ Differences in magnitude between predictions versus observed data suggest that ABR may be higher than assumed.
- ✓ Future work should extend age of OAE onset and explore the relationship between ABR and OAE incidence.
- ✓ OAE dynamics are highly resilient to ivermectin treatment, in no small part due to very high baseline mf prevalence.
- ✓ Exclusion of under 5’s from ivermectin MDA programmes should be reconsidered.

References

- Chesnais CB, Nana-Djeunga HC, Njamnshi AK, Lenou-Nanga CG, Boullé C, Bissek AC, Kamgno J, Colebunders R, Boussinesq M. The temporal relationship between onchocerciasis and epilepsy: a population-based cohort study. *Lancet Infect Dis*. 2018 18(11): 1278-86.
- Hamley JI, Milton P, Walker M, Basáñez MG. Modelling exposure heterogeneity and density dependence in onchocerciasis using a novel individual-based transmission model, EPIONCHO-IBM: Implications for elimination and data needs. *PLoS Negl Trop Dis* 2019;13(12): e0007557.
- Basáñez MG, Pion SDS, Churcher TS, Breitling LP, Little MP, Boussinesq M. River blindness: A success story under threat? *PLoS Med*. 2006; 3(9): e371.

Photo Credits: Community Eye Health Journal