Delaying age of infection: a pernicious effect of vector control

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Overview

Key facts from WHO about Zyka virus

- Zika virus disease is caused by a virus transmitted primarily by Aedes mosquitoes, which bite during the day.

Key facts from WHO about Zyka virus

- Symptoms are generally mild and include fever, rash, conjunctivitis, muscle and joint pain, malaise or headache. Symptoms typically last for 2–7 days. Most people with Zika virus infection do not develop symptoms.

Key facts from WHO about Zyka virus

- Zika virus infection during pregnancy can cause infants to be born with microcephaly and other congenital malformations, known as congenital Zika syndrome. Infection with Zika virus is also associated with other complications of pregnancy including preterm birth and miscarriage.
- An increased risk of neurologic complications is associated with Zika virus infection in adults and children, including Guillain-Barré syndrome, neuropathy and myelitis.

Key facts from WHO about Zyka virus

- Zika virus was identified in humans in 1952 in Uganda and the United Republic of Tanzania.
- Outbreaks of Zika virus disease have been recorded in Africa, the Americas, Asia and the Pacific. From the 1960s to 1980s, rare sporadic cases of human infections were found across Africa and Asia, typically accompanied by mild illness.

Key facts from WHO about Zyka virus

- The first recorded outbreak of Zika virus disease was reported from the Island of Yap (Federated States of Micronesia) in 2007. This was followed by a large outbreak of Zika virus infection in French Polynesia in 2013 and other countries and territories in the Pacific.
- In March 2015, Brazil reported a large outbreak of rash illness, soon identified as Zika virus infection, and in July 2015, found to be associated with Guillain-Barré syndrome. In October 2015, Brazil reported an association between Zika virus infection and microcephaly.

Key facts from WHO about Zyka virus

- Outbreaks and evidence of transmission soon appeared throughout the Americas, Africa, and other regions of the world.
- To date, a total of 86 countries and territories have reported evidence of mosquito-transmitted Zika infection.

Our question

What would happen in the countries where Zika virus is present with mostly asymptomatic and mild illness, if they start controlling the Aedes mosquitoes, motivated by Dengue control?

The model SEIR-SEI

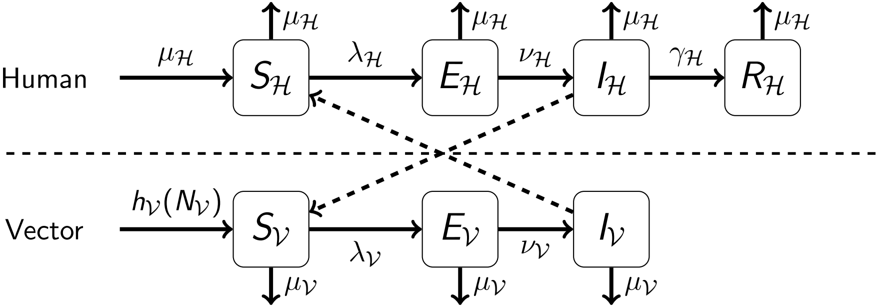

Figure: SEIR-SEI model for Zika disease[1]

[1] We choose a SEIR-SEI model based on the overview by Wiratsudakul, Suparit and Modchang, 2018. This one follows Manore et al, 2014 and Xue et al, 2017

The equations

$$
\begin{aligned}
S'_{\mathcal{H}} &= \mu_{\mathcal{H}} N_{\mathcal{H}} - \lambda_{\mathcal{H}}(t) S_{\mathcal{H}} - \mu_{\mathcal{H}} S_{\mathcal{H}} \\
E'_{\mathcal{H}} &= \lambda_{\mathcal{H}}(t) S_{\mathcal{H}} - \nu_{\mathcal{H}} E_{\mathcal{H}} - \mu_{\mathcal{H}} E_{\mathcal{H}} \\
I'_{\mathcal{H}} &= \nu_{\mathcal{H}} E_{\mathcal{H}} - \gamma_{\mathcal{H}} I_{\mathcal{H}} - \mu_{\mathcal{H}} I_{\mathcal{H}} \\
R'_{\mathcal{H}} &= \gamma_{\mathcal{H}} I_{\mathcal{H}} - \mu_{\mathcal{H}} R_{\mathcal{H}} \\
S'_{\mathcal{V}} &= h_{\mathcal{V}}(N_{\mathcal{V}}) N_{\mathcal{V}} - \lambda_{\mathcal{V}}(t) S_{\mathcal{V}} - \mu_{\mathcal{V}} S_{\mathcal{V}} \\
E'_{\mathcal{V}} &= \lambda_{\mathcal{V}}(t) S_{\mathcal{V}} - \nu_{\mathcal{V}} E_{\mathcal{V}} - \mu_{\mathcal{V}} E_{\mathcal{V}} \\
I'_{\mathcal{V}} &= \nu_{\mathcal{V}} E_{\mathcal{V}} - \mu_{\mathcal{V}} I_{\mathcal{V}}
\end{aligned}
$$

$$
\begin{aligned}
h_{\mathcal{V}}(N_{\mathcal{V}}) &= \Psi_{\mathcal{V}} - \tfrac{\Psi_{\mathcal{V}} - \mu_{\mathcal{V}}}{K_{\mathcal{V}}} N_{\mathcal{V}} \\
\lambda_{\mathcal{H}}(t) &= \tfrac{\sigma_{\mathcal{V}} \sigma_{\mathcal{H}} N_{\mathcal{V}}}{\sigma_{\mathcal{V}} N_{\mathcal{V}} + \sigma_{\mathcal{H}} N_{\mathcal{H}}} \beta_{\mathcal{H}\mathcal{V}} \tfrac{I_{\mathcal{V}}}{N_{\mathcal{V}}} \\
\lambda_{\mathcal{V}}(t) &= \tfrac{\sigma_{\mathcal{V}} \sigma_{\mathcal{H}} N_{\mathcal{V}}}{\sigma_{\mathcal{V}} N_{\mathcal{V}} + \sigma_{\mathcal{H}} N_{\mathcal{H}}} \beta_{\mathcal{V}\mathcal{H}} \tfrac{I_{\mathcal{H}}}{N_{\mathcal{H}}}
\end{aligned}
$$

The basic reproduction number

Define

$$
\begin{aligned}
R_{\mathcal{H}\mathcal{V}} &= \frac{\nu_{\mathcal{V}}}{\mu_{\mathcal{V}}+\nu_{\mathcal{V}}}\frac{\sigma_{\mathcal{V}}}{\mu_{\mathcal{V}}}\frac{\sigma_{\mathcal{H}}N_{\mathcal{H}}}{\sigma_{\mathcal{H}}N_{\mathcal{H}}+\sigma_{\mathcal{V}}K_{\mathcal{V}}}\beta_{\mathcal{H}\mathcal{V}} \\
R_{\mathcal{V}\mathcal{H}} &= \frac{\nu_{\mathcal{H}}}{\mu_{\mathcal{H}}+\nu_{\mathcal{H}}}\frac{\sigma_{\mathcal{H}}}{\mu_{\mathcal{H}}+\gamma_{\mathcal{H}}}\frac{\sigma_{\mathcal{V}}K_{\mathcal{V}}}{\sigma_{\mathcal{H}}N_{\mathcal{H}}+\sigma_{\mathcal{V}}K_{\mathcal{V}}}\beta_{\mathcal{V}\mathcal{H}}
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$$

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Define

$$R_{\mathcal{H}\mathcal{V}} = \frac{\nu_{\mathcal{V}}}{\mu_{\mathcal{V}}+\nu_{\mathcal{V}}}\frac{\sigma_{\mathcal{V}}}{\mu_{\mathcal{V}}}\frac{\sigma_{\mathcal{H}}N_{\mathcal{H}}}{\sigma_{\mathcal{H}}N_{\mathcal{H}}+\sigma_{\mathcal{V}}K_{\mathcal{V}}}\beta_{\mathcal{H}\mathcal{V}}$$

$$R_{\mathcal{V}\mathcal{H}} = \frac{\nu_{\mathcal{H}}}{\mu_{\mathcal{H}}+\nu_{\mathcal{H}}}\frac{\sigma_{\mathcal{H}}}{\mu_{\mathcal{H}}+\gamma_{\mathcal{H}}}\frac{\sigma_{\mathcal{V}}K_{\mathcal{V}}}{\sigma_{\mathcal{H}}N_{\mathcal{H}}+\sigma_{\mathcal{V}}K_{\mathcal{V}}}\beta_{\mathcal{V}\mathcal{H}}$$

Then

$$\mathcal{R}_0 = \sqrt{R_{\mathcal{H}\mathcal{V}}R_{\mathcal{V}\mathcal{H}}}$$

The endemic equilibrium

if $\mathcal{R}_0 > 1$, there is an endemic equilibrium given by

$$\begin{aligned}
S_{\mathcal{H}}^* &= N_{\mathcal{H}} \left(1 - \left(1 - \frac{1}{\mathcal{R}_0^2}\right) M_{\mathcal{H}}\right) \\
E_{\mathcal{H}}^* &= N_{\mathcal{H}} \left(1 - \frac{1}{\mathcal{R}_0^2}\right) M_{\mathcal{H}} \frac{\mu_{\mathcal{H}}}{\mu_{\mathcal{H}}+\nu_{\mathcal{H}}} \\
I_{\mathcal{H}}^* &= N_{\mathcal{H}} \left(1 - \frac{1}{\mathcal{R}_0^2}\right) M_{\mathcal{H}} \frac{\nu_{\mathcal{H}}}{\mu_{\mathcal{H}}+\nu_{\mathcal{H}}} \frac{\mu_{\mathcal{H}}}{\mu_{\mathcal{H}}+\gamma_{\mathcal{H}}} \\
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S_{\mathcal{V}}^* &= K_{\mathcal{V}} \left(1 - \left(1 - \frac{1}{\mathcal{R}_0^2}\right) M_{\mathcal{V}}\right) \\
E_{\mathcal{V}}^* &= K_{\mathcal{V}} \left(1 - \frac{1}{\mathcal{R}_0^2}\right) M_{\mathcal{V}} \frac{\mu_{\mathcal{V}}}{\mu_{\mathcal{V}}+\nu_{\mathcal{V}}} \\
I_{\mathcal{V}}^* &= K_{\mathcal{V}} \left(1 - \frac{1}{\mathcal{R}_0^2}\right) M_{\mathcal{V}} \frac{\nu_{\mathcal{V}}}{\mu_{\mathcal{V}}+\nu_{\mathcal{V}}}
\end{aligned}$$

for $M_{\mathcal{H}} = \frac{\frac{R_{\mathcal{H}\mathcal{V}}\mu_{\mathcal{V}}K_{\mathcal{V}}}{\mu_{\mathcal{H}}N_{\mathcal{H}}}}{1+\frac{R_{\mathcal{H}\mathcal{V}}\mu_{\mathcal{V}}K_{\mathcal{V}}}{\mu_{\mathcal{H}}N_{\mathcal{H}}}}$ and $M_{\mathcal{V}} = \frac{\frac{R_{\mathcal{V}\mathcal{H}}\mu_{\mathcal{H}}N_{\mathcal{H}}}{\mu_{\mathcal{V}}K_{\mathcal{V}}}}{1+\frac{R_{\mathcal{V}\mathcal{H}}\mu_{\mathcal{H}}N_{\mathcal{H}}}{\mu_{\mathcal{V}}K_{\mathcal{V}}}}$

Manore et al (2014) conjectured that the endemic equilibrium is locally asymptotically stable

Cohort

Consider the system in the endemic equilibrium and take a cohort of the human population containing the newborns in a given year

The EDO system for the cohort

Reduces to a linear system

$$
\begin{aligned}
S' &= -\beta S - \mu S \\
E' &= \beta S - (\nu + \mu) E \\
I' &= \nu E - (\gamma + \mu) I \\
R' &= \gamma I - \mu R
\end{aligned}
$$

The EDO system for the cohort

Reduces to a linear system

$$\begin{aligned} S' &= -\beta S - \mu S \\ E' &= \beta S - (\nu + \mu)E \\ I' &= \nu E - (\gamma + \mu)I \\ R' &= \gamma I - \mu R \end{aligned}$$

with proper initial conditions, like $S_0 = \mu_{\mathcal{H}} N_{\mathcal{H}}, E_0 = I_0 = R_0 = 0$

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$$\begin{array}{rcl} S' & = & -\beta S - \mu S \\ E' & = & \beta S - (\nu + \mu) E \\ I' & = & \nu E - (\gamma + \mu) I \\ R' & = & \gamma I - \mu R \end{array}$$

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and $\beta = \lambda^*_{\mathcal{H}} = \frac{\sigma_{\mathcal{V}} \sigma_{\mathcal{H}} N_{\mathcal{V}}}{\sigma_{\mathcal{V}} N_{\mathcal{V}} + \sigma_{\mathcal{H}} N_{\mathcal{H}}} \beta_{\mathcal{H}\mathcal{V}} \frac{I^*_{\mathcal{V}}}{N_{\mathcal{V}}}$

Remember the original system

$$
\begin{aligned}
S'_{\mathcal{H}} &= \mu_{\mathcal{H}} N_{\mathcal{H}} - \lambda_{\mathcal{H}}(t) S_{\mathcal{H}} - \mu_{\mathcal{H}} S_{\mathcal{H}} \\
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Solution of the cohort linear system

We get the solution

$S = S_\beta(t) = S_0 \mathrm{e}^{-(\beta+\mu)t}$

$E = E_\beta(t) = S_0 \frac{\beta}{\nu-\beta} \mathrm{e}^{-(\beta+\mu+\nu)t} \left(\mathrm{e}^{\nu t} - \mathrm{e}^{\beta t}\right)$

...

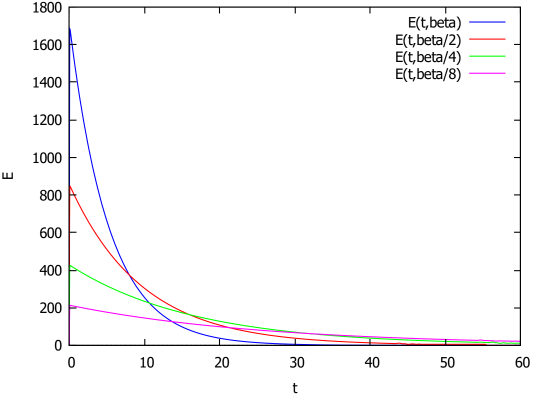


Figure: E as a function of time for several scales of β

Exposed in fertile age

$$E_{fertile}(\beta) = \int_a^b E_\beta(t)\,dt =$$
$$S_0 \frac{\beta}{\nu-\beta}\left[\frac{1}{\nu+\mu}\left(\mathrm{e}^{-(\nu+\mu)b} - \mathrm{e}^{-(\nu+\mu)a}\right) + \frac{1}{\beta+\mu}\left(\mathrm{e}^{-(\beta+\mu)a} - \mathrm{e}^{-(\beta+\mu)b}\right)\right]$$

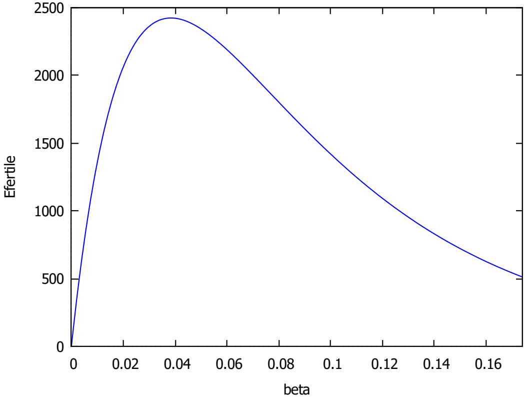
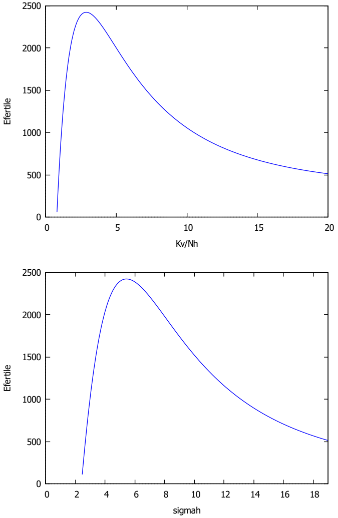


Figure: $E_{fertile}$ as a function β

$E_{fertile}$ as a function of vector control parameters



Conclusions

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- The analysis is done at the endemic equilibrium, discarding the transient behavior of the system
- For all parameters analyzed we conclude that there is an increase of exposed in fertile age
- We would like to find a strategy that allow to control the vector without increasing the exposed in fertile age. How?

An invitation

eventos.fct.unl.pt/3epb

Thank you