

Supplemental Information

Supplemental Information I:

Figure S1 shows the basic elements of our ZIKV model. Transition rates between states, along with ranges for these parameters, can be found in Table One of the main text.

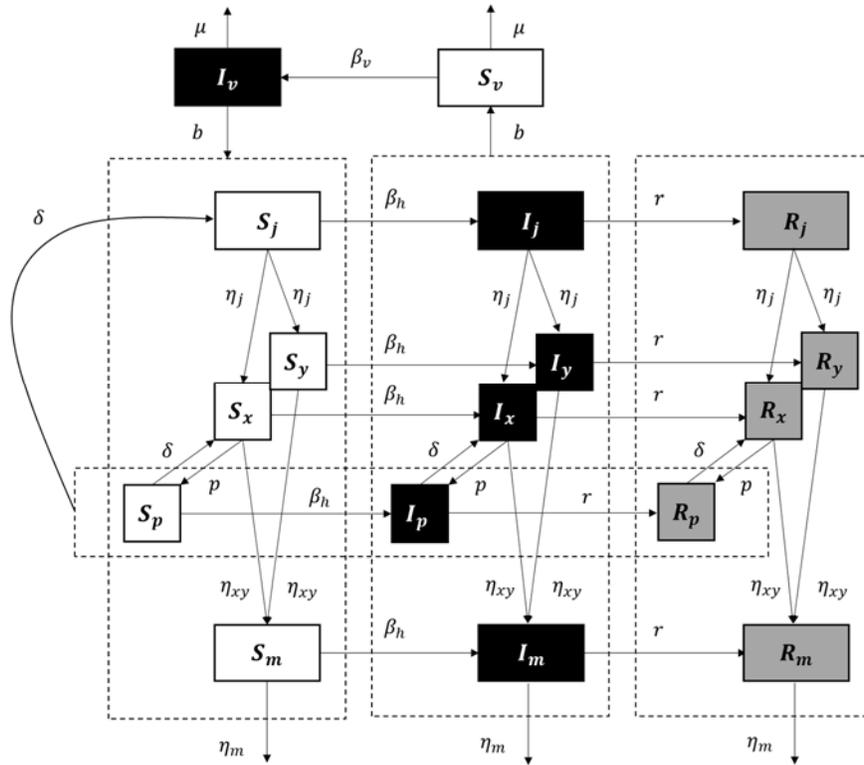
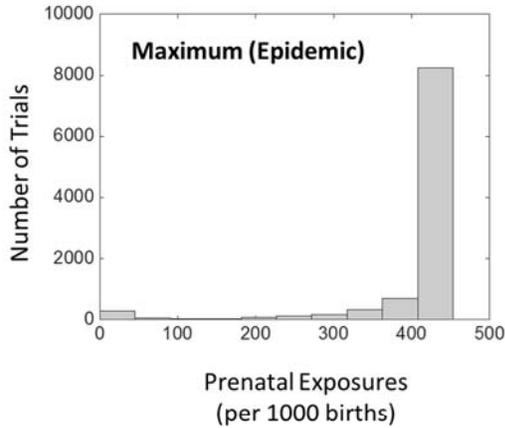


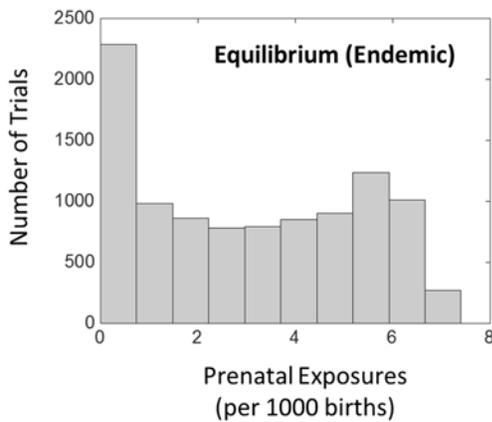
Figure S1 Schematic illustrating transitions between the different compartments in our model. The human host population can be susceptible (white), infected (black) or recovered (grey), while the vector population is either susceptible (white) or infected (black). For the human population, subscripts indicate the following: j for children, x for reproductive females that are not pregnant, p for reproductive females that are pregnant, y for reproductive males and m for post-reproductive adults. Dashed boxes demark classes with shared transitions.

Supplemental Information II

A.



B.



C.

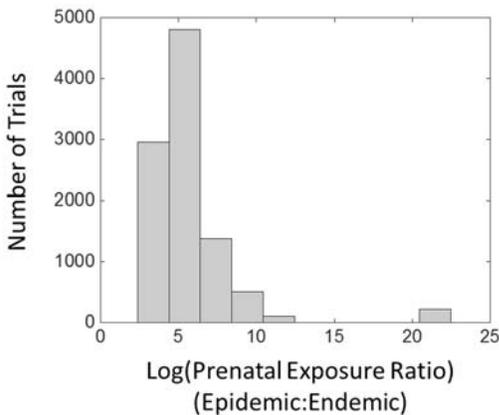


Figure S2 shows histograms summarizing results from our Latin Hypercube Sampling (LHS) analysis. Notice that the majority of scenarios predict maximum prenatal exposure rates >400 per 1000 births. By contrast, equilibrium scenarios predict prenatal exposure rates <10 per 1000 births. The dramatic reduction from epidemic scenarios (shortly after ZIKV is introduced into a region) to endemic scenarios (after the virus has been circulating for long periods of time) is further highlighted by the ratio of maximum prenatal exposure rate to equilibrium prenatal exposure rate, which shows that most systems exhibit a ~ 150 -fold decrease in going from epidemic to endemic conditions.

Figure S2 Histograms showing the number of LHS trials with given (a) maximum prenatal exposure rates (b) equilibrium prenatal exposure rates and (c) maximum:equilibrium prenatal exposure rates. LHS sampling was over the ranges in Table One, but assuming the following restrictions to ensure monotonicity: $b \in (0.4, 1)$, $A \in (1000, 5000)$ and $\beta_h \in (0.15, 0.75)$.

Supplemental Information III:

To explore the incidence of microcephaly in the case that high risk is only associated with ZIKV infection during the early stages of pregnancy, we divide the pregnancy class in equations (1-6) into two separate stages, as follows:

Pre-reproductive females and males:

$$\frac{dS_j}{dt} = \overbrace{\delta_2(S_{p,2} + I_{p,2} + R_{p,2})}^{\text{birth}} - \overbrace{\eta_j \widehat{S}_j}^{\text{maturation}} - \overbrace{\frac{\beta_{hb}}{N_h} S_j I_v}^{\text{infection}} \quad (\text{S3.1})$$

Reproductive females (not pregnant):

$$\frac{dS_x}{dt} = \overbrace{\frac{\eta_j}{2} \widehat{S}_j}^{\text{maturation}} - \overbrace{\eta_{xy} \widehat{S}_x}^{\text{maturation}} - \overbrace{p \widehat{S}_x}^{\text{pregnancy}} + \overbrace{\delta_2 \widehat{S}_{p,2}}^{\text{delivery}} - \overbrace{\frac{\beta_{hb}}{N_h} S_x I_v}^{\text{infection}} \quad (\text{S3.2.a})$$

$$\frac{dI_x}{dt} = \overbrace{\frac{\eta_j}{2} \widehat{I}_j}^{\text{maturation}} - \overbrace{\eta_{xy} \widehat{I}_x}^{\text{maturation}} - \overbrace{p \widehat{I}_x}^{\text{pregnancy}} + \overbrace{\delta_2 \widehat{I}_{p,2}}^{\text{delivery}} + \overbrace{\frac{\beta_{hb}}{N_h} S_x I_v}^{\text{infection}} - \overbrace{r \widehat{I}_x}^{\text{recovery}} \quad (\text{S3.2.b})$$

$$\frac{dR_x}{dt} = \overbrace{\frac{\eta_j}{2} \widehat{R}_j}^{\text{maturation}} - \overbrace{\eta_{xy} \widehat{R}_x}^{\text{maturation}} - \overbrace{p \widehat{R}_x}^{\text{pregnancy}} + \overbrace{\delta_2 \widehat{R}_{p,2}}^{\text{delivery}} + \overbrace{r \widehat{I}_x}^{\text{recovery}} \quad (\text{S3.2.c})$$

Reproductive females (pregnant, at risk):

$$\frac{dS_{p,1}}{dt} = \overbrace{p \widehat{S}_x}^{\text{pregnancy}} - \overbrace{\delta_1 \widehat{S}_{p,1}}^{\text{leaving risk stage}} - \overbrace{\frac{\beta_{hb}}{N_h} S_{p,1} I_v}^{\text{infection}} \quad (\text{S3.3.a})$$

$$\frac{dI_{p,1}}{dt} = \overbrace{p \widehat{I}_x}^{\text{pregnancy}} - \overbrace{\delta_1 \widehat{I}_{p,1}}^{\text{leaving risk stage}} + \overbrace{\frac{\beta_{hb}}{N_h} S_{p,1} I_v}^{\text{infection}} - \overbrace{r \widehat{I}_{p,1}}^{\text{recovery}} \quad (\text{S3.3.b})$$

$$\frac{dR_{p,1}}{dt} = \overbrace{p \widehat{R}_x}^{\text{pregnancy}} - \overbrace{\delta_1 \widehat{R}_{p,1}}^{\text{leaving risk stage}} + \overbrace{r \widehat{I}_{p,1}}^{\text{recovery}} \quad (\text{S3.3.c})$$

Reproductive females (pregnant, not at risk):

$$\frac{dS_{p,2}}{dt} = \overbrace{\delta_1 \widehat{S}_{p,1}}^{\text{leaving risk stage}} - \overbrace{\frac{\beta_{hb}}{N_h} S_{p,2} I_v}^{\text{infection}} - \overbrace{\delta_2 \widehat{S}_{p,2}}^{\text{delivery}} \quad (\text{S3.3.a})$$

$$\frac{dI_{p,2}}{dt} = \overbrace{\delta_1 I_{p,1}}^{\text{leaving risk stage}} + \overbrace{\frac{\beta_{hb}}{N_h} S_{p,2} I_v}_{\text{infection}} - \overbrace{r I_{p,2}}^{\text{recovery}} - \overbrace{\delta_2 I_{p,2}}^{\text{delivery}} \quad (\text{S3.3.b})$$

$$\frac{dR_{p,2}}{dt} = \overbrace{\delta_1 R_{p,1}}^{\text{leaving risk stage}} + \overbrace{r I_{p,2}}^{\text{recovery}} - \overbrace{\delta_2 R_{p,2}}^{\text{delivery}} \quad (\text{S3.3.c})$$

Mosquitoes:

$$\frac{dS_v}{dt} = A - \overbrace{\mu S_v}^{\text{death}} - \overbrace{\frac{\beta_{vb}}{N_h} S_v (I_j + I_x + I_{p,1} + I_{p,2} + I_y + I_m)}^{\text{infection}} \quad (\text{S3.4.a})$$

$$\frac{dI_v}{dt} = -\overbrace{\mu I_v}^{\text{death}} + \overbrace{\frac{\beta_{vb}}{N_h} S_v (I_j + I_x + I_{p,1} + I_{p,2} + I_y + I_m)}^{\text{infection}} \quad (\text{S3.4.b})$$

where we have only shown those equations that are modified, and where the total length of the gestation period is given by $1/\delta_1 + 1/\delta_2$. Figure S2 shows how the length of the high risk period affects both the maximum (epidemic) and equilibrium (endemic) rates of high risk ZIKV exposures. As expected, shorter high risk periods result in lower numbers of high risk exposures, with a nearly linear relationship between the length of the high risk period and the exposure rate. Despite this, we see that even if high risk is only associated with ZIKV infection during the first trimester, over 10% of pregnant women will experience a high risk ZIKV infection during an epidemic. Under endemic conditions, the risk is closer to 0.1%.

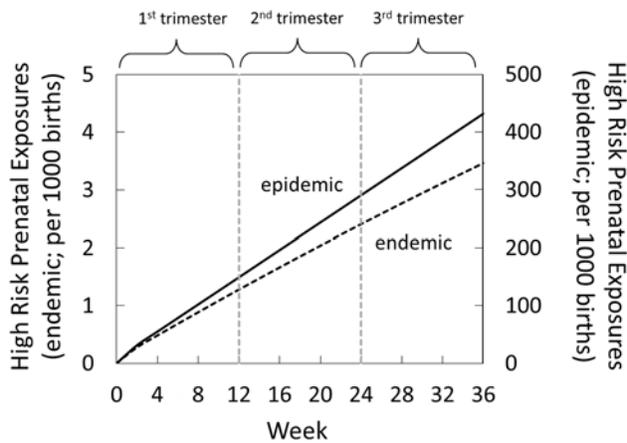


Figure S3 The number of high risk prenatal exposures as a function of the length of the high risk period for systems where ZIKV has been newly introduced (epidemic, solid) and systems where ZIKV has been circulating for many years (endemic, dashed). We assume average values for all parameters (see Table One) except the gestation period, which is broken into a high risk period and a low risk period, always totaling 9 months. Note that the y-axes for epidemic and endemic dynamics differ by 100-fold.

Supplemental Information IV:

To explore the effect of population growth, we consider prenatal exposures at long time-points ($t = 500$) for growing populations (note that growing populations will not reach an equilibrium). For these scenarios, we begin with $N_h = 10000$, and an age-distribution consistent with an equilibrium population. We then allow the population to grow ($p = 2.1\eta_{xy}$), considering similar dependencies as in Figure 3 of the main text. Results are shown in Figure S4. From this figure, it is clear that the same qualitative trends in prenatal exposures that we observed in steady-state populations also hold in systems with growing populations.

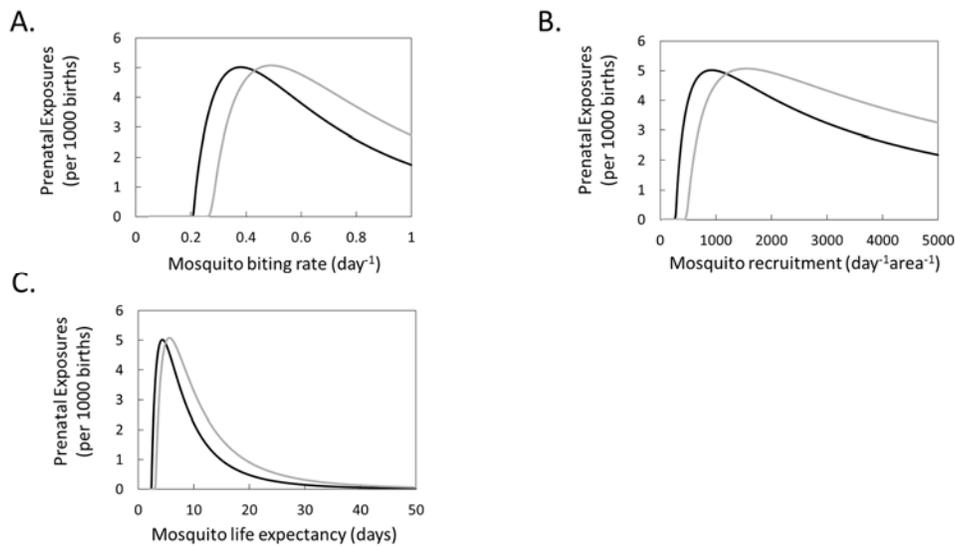


Figure S4 Number of women who experience an active ZIKV infection at any point during pregnancy as a function of (a) mosquito biting rates, (b) mosquito recruitment rates and (c) mosquito life expectancy in a region with endemic disease (i.e., a system at equilibrium) for a population of constant size (black) and an increasing population (grey). In each panel, we assume average values for all parameters except the one being varied (see Table One).

Supplementary Information V

Figure S5 shows monotonicity plots for endemic prenatal exposures against each of the 11 variables in our LHS matrix. From this figure, we see that b , A , and β_h are obviously non-monotonic at low values. Therefore, to perform PRCC analysis, we restrict the ranges of these parameters to $b \in (0.4, 1)$, $A \in (1000, 5000)$ and $\beta_h \in (0.15, 0.75)$ respectively. This means that LHS results only apply under the assumption that mosquito biting rates, mosquito recruitment and mosquito-to-human transmission are reasonably high (in practice, high enough to prevent $R_0 \approx 1$). Restricting the ranges of mosquito biting rates, mosquito recruitment rates and mosquito-to-human transmission removes the slight non-monotonicity observed in η_{xy} and μ , so we use the full range for these two parameters.

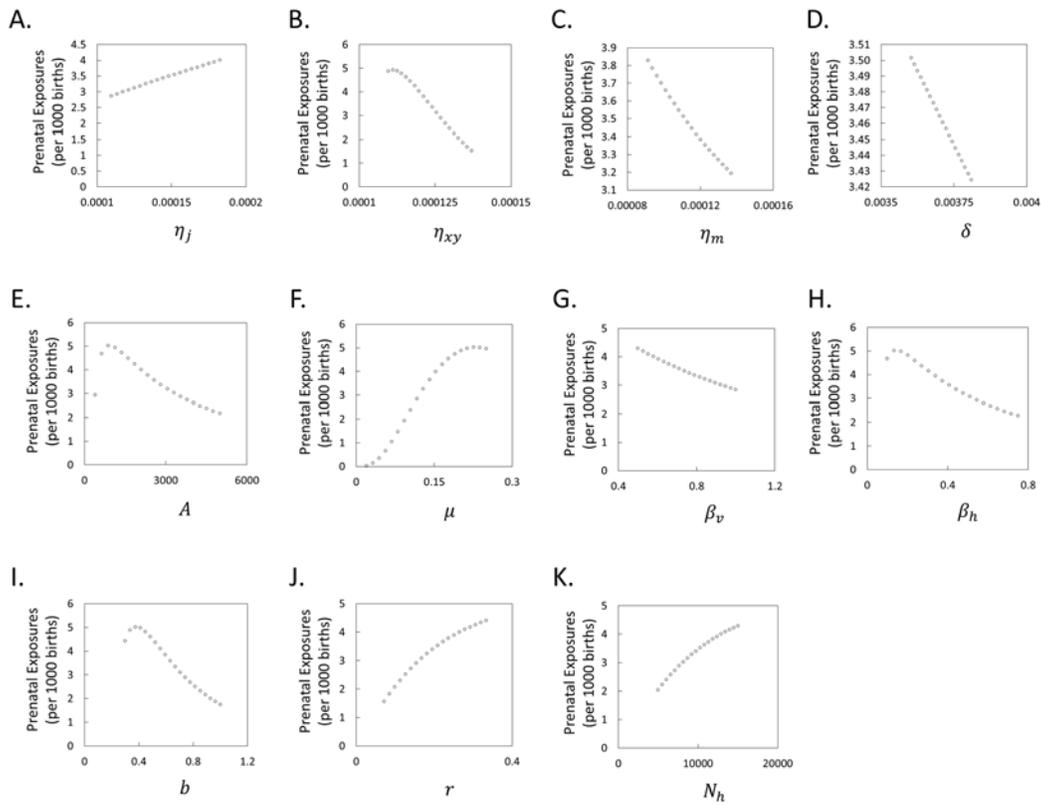


Figure S5 Monotonicity plots for endemic prenatal exposures against the 11 variables in our LHS analysis. In each panel, we assume average values for all parameters except the one being varied (see Table One).