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The Temperature Sensitivity of Arboviral Disease Extrinsic Incubation Periods: A Systematic Review and Bayesian Time Delay Modelling Study

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Start Presentation

Arboviruses: An Overview



Public Health Burden

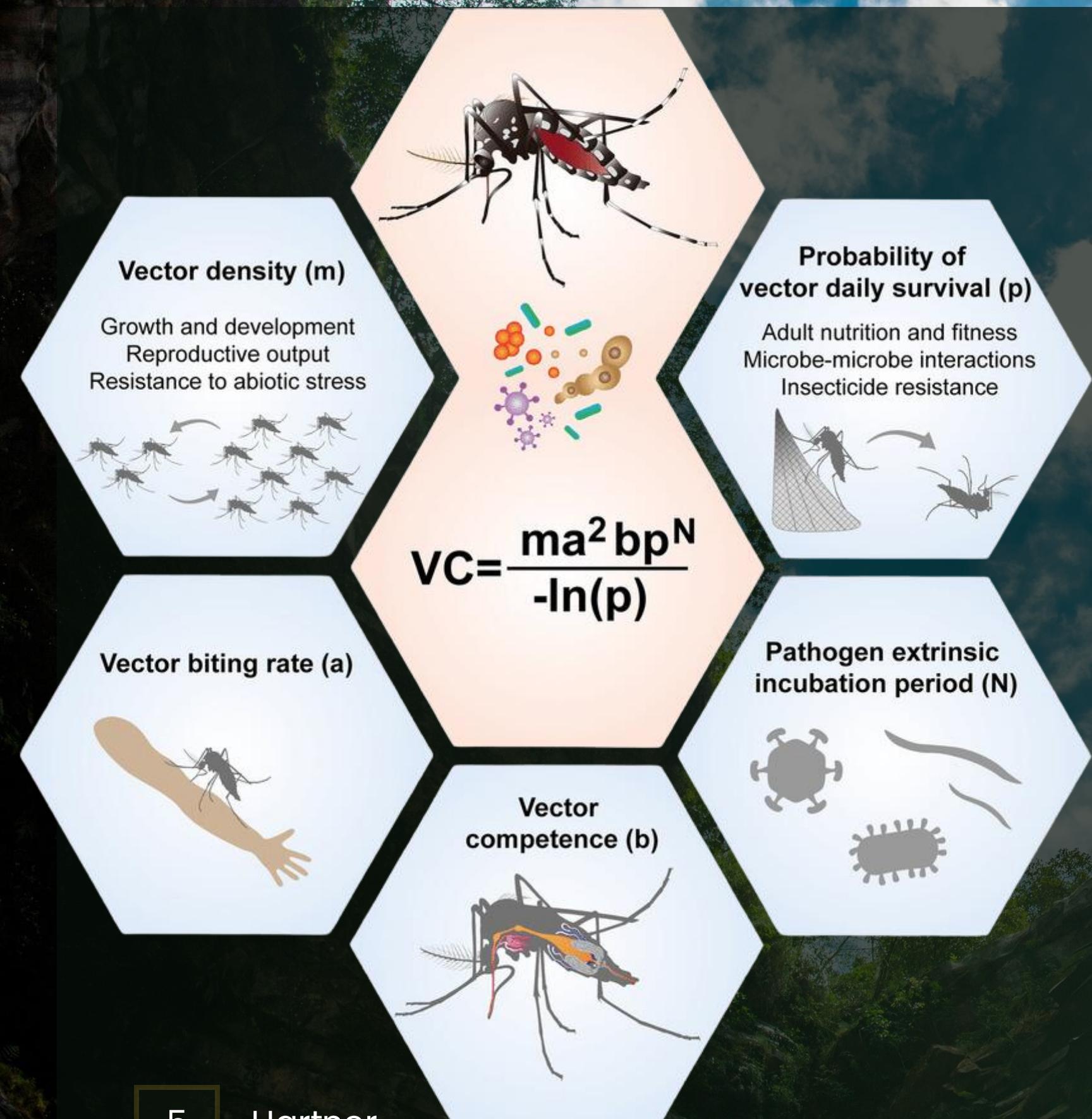
- Major public health threat in tropical and sub-tropical regions (pop. 4 billion)
- Dengue alone caused 6.5 million infections in 2023
- Infection can lead to severe neuroinvasive disease or death

Transmission Drivers

- Human host availability and susceptibility
- Viral Factors
- Vectorial capacity (transmission potential of vector-pathogen)
- Environmental Factors (Climate Change)

Vectorial Capacity

- Temperature greatly affects the
 - Gonotrophic cycle (m, a)
 - Mosquito survival on infection (p, n)
 - Vector competence (b)
- Thermal optima and limits vary across vector-pathogen systems



5

Hartner

Cansado-Utrilla et al. (2021). The microbiome and mosquito vectorial capacity: rich potential for discovery and translation. *Microbiome*. 9. 10.1186/s40168-021-01073-2.



Defining EIP



Extrinsic Incubation Period

Time it takes for a virus to disseminate through a mosquito from the midgut where virus enters the mosquito after blood feeding to the salivary glands where it is then expectorated upon subsequent feeding

EIP: Importance and Data Limitations



Understand overall transmission efficiency



Outbreaks: EIP plays a crucial role in the dynamics and magnitude of outbreaks



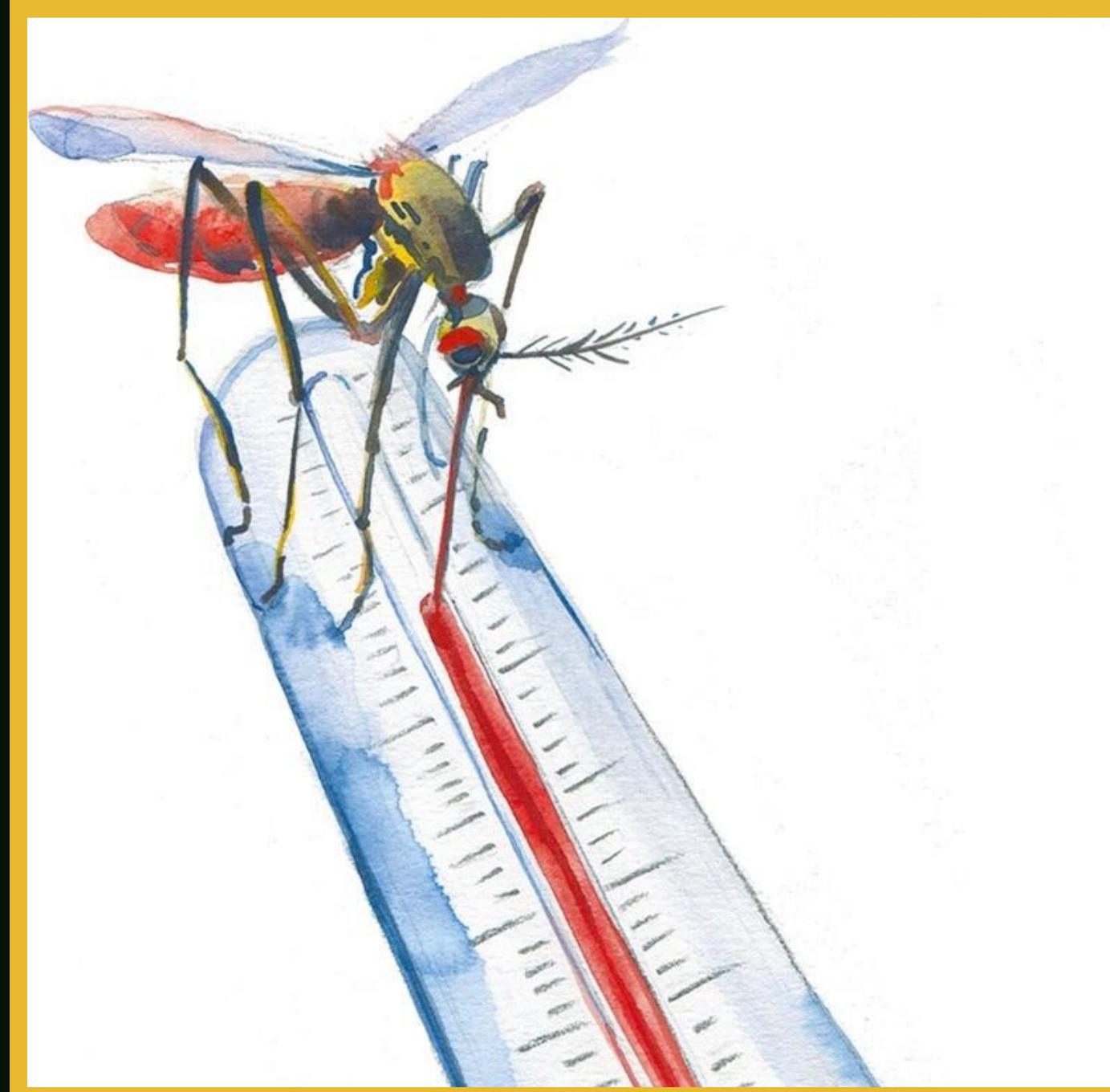
Challenges of working with live viruses; lack of studies for some disease areas



Poor data reporting: No cohort sizes reported or low sample sizes



Understanding EIP parameter estimates



Aims

1. Understand link between climatatic variables (T, humidity, etc) and EIP for all arboviral disease areas for which there is data availability
2. Generate narrative evidence across studies for which data extraction is not possible

Details

TIMELINE: January 2024 - May 2025

PARTICIPANTS: Christopher Irrgang, Tim Herath, Nils Körber, Luis Roger Esquivel Gomez, Juliane Pfeil, Jean-Baptiste Escudié

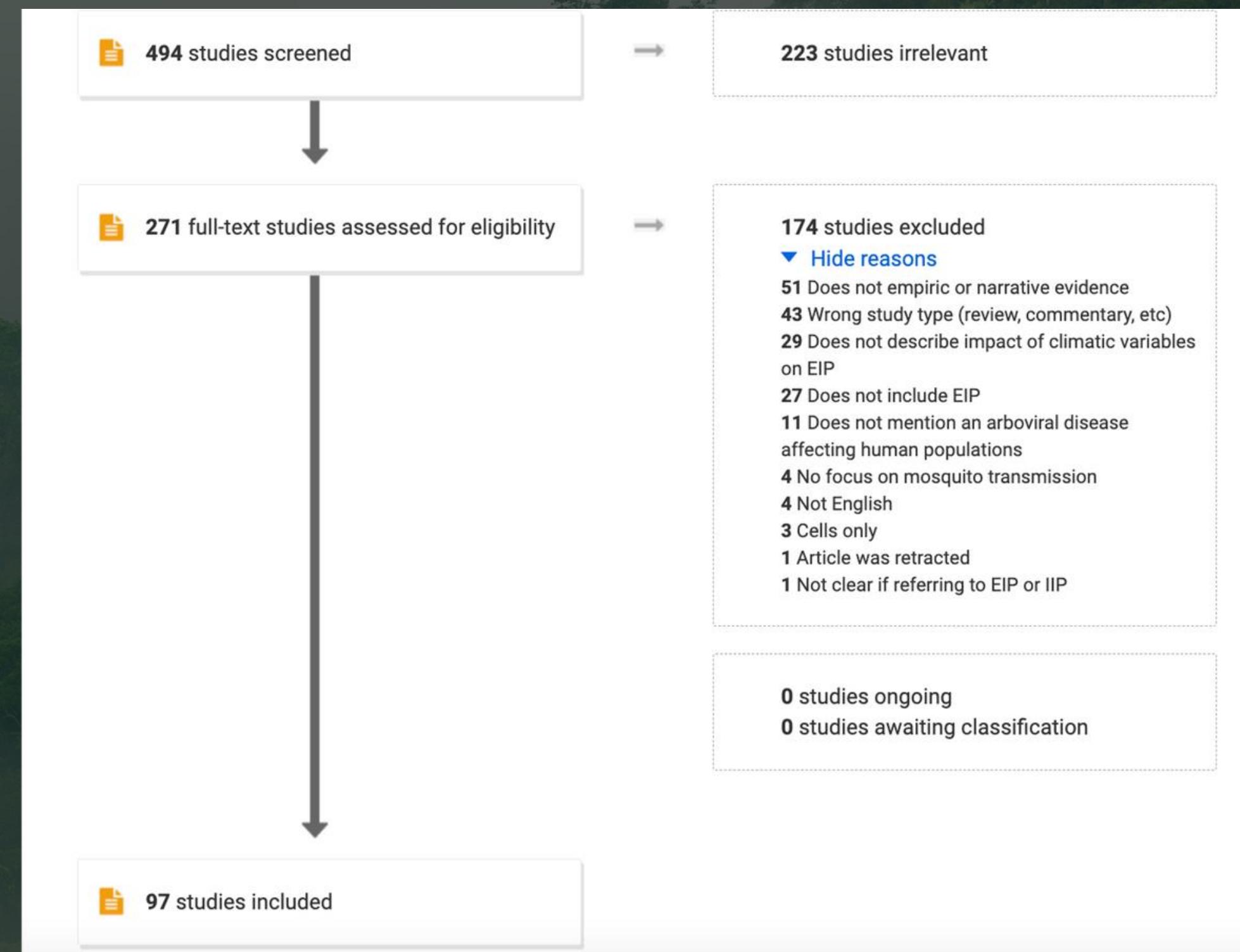


The Study

- **Systematic Review:** 97 included studies from 3 databases on arboviral diseases in humans
- Must have focused on impact of climate on EIP in mosquito vectors
- 2 reviewer system to verify all data

Extracted:

- SG and Transmission Data
- Feeding vs injection data
- Mosquito origin
- Viral Strain



Virus	Genus	Vector Species	Countries Represented	Observations	Study Years
WNV (West Nile virus)	<i>Flavivirus</i>	Ae. japonicus, Ae. vexans, Cx. pipiens molestus, Cx. pipiens pipiens, Cx. pipiens pipiens/molestus, Cx. quinquefasciatus, Cx. restuans, Cx. tarsalis, Cx. torrentium	Germany, Italy, Switzerland, The Netherlands, United States	5507	2010-2021
MVEV (Murray Valley encephalitis virus)	<i>Flavivirus</i>	Ae. alboannulatus, Ae. sagax, Cx. annulirostris	Australia	647	1989
ZIKV (Zika virus)	<i>Flavivirus</i>	Ae. aegypti, Ae. albopictus, Ae. japonicus	Australia, Brazil, France, Germany, Mexico, Switzerland, United States	7295	2018-2020
DENV (Dengue virus)	<i>Flavivirus</i>	Ae. aegypti, Ae. albopictus	Argentina, China, Taiwan, Thailand, United States	912	1987-2017
SLEV (St. Louis encephalitis virus)	<i>Flavivirus</i>	Cx. nigripalpus	United States	122	2012
JEV (Japanese encephalitis virus)	<i>Flavivirus</i>	Cs. annulata, Cx. pipiens, Cx. quinquefasciatus, Oc. detritus	Brazil, United States	398	2015-2021
MAYV (Mayaro virus)	<i>Alphavirus</i>	Ae. aegypti	United States	300	2022
CHIKV (Chikungunya virus)	<i>Alphavirus</i>	Ae. aegypti, Ae. albopictus	Australia, Germany, Italy, Switzerland, United States	1083	2018-2023
VEEV (Venezuelan equine encephalitis virus)	<i>Alphavirus</i>	Oc. detritus	United Kingdom	300	2020
WEE (Western equine encephalitis virus)	<i>Alphavirus</i>	Cx. tarsalis	United States	175	1983
GETV (Getah virus)	<i>Alphavirus</i>	Ae. vexans niponii, Cx. tritaeniorhynchus	Japan	80	1985
RRV (Ross River virus)	<i>Alphavirus</i>	Oc. detritus, Oc. vigilax	Australia, United Kingdom	914	2002-2020
RVFV (Rift Valley fever virus)	<i>Phlebovirus</i>	Ae. albopictus, Cx. pipiens pipiens/molestus	Spain	200	2017
CEV (California encephalitis virus)	<i>Orthobunyavirus</i>	Ae. communis, Ae. aegypti	Canada	55	1974-1977

Salivary Gland Data*

14 diseases across
17 countries

Nearly 21k
observations

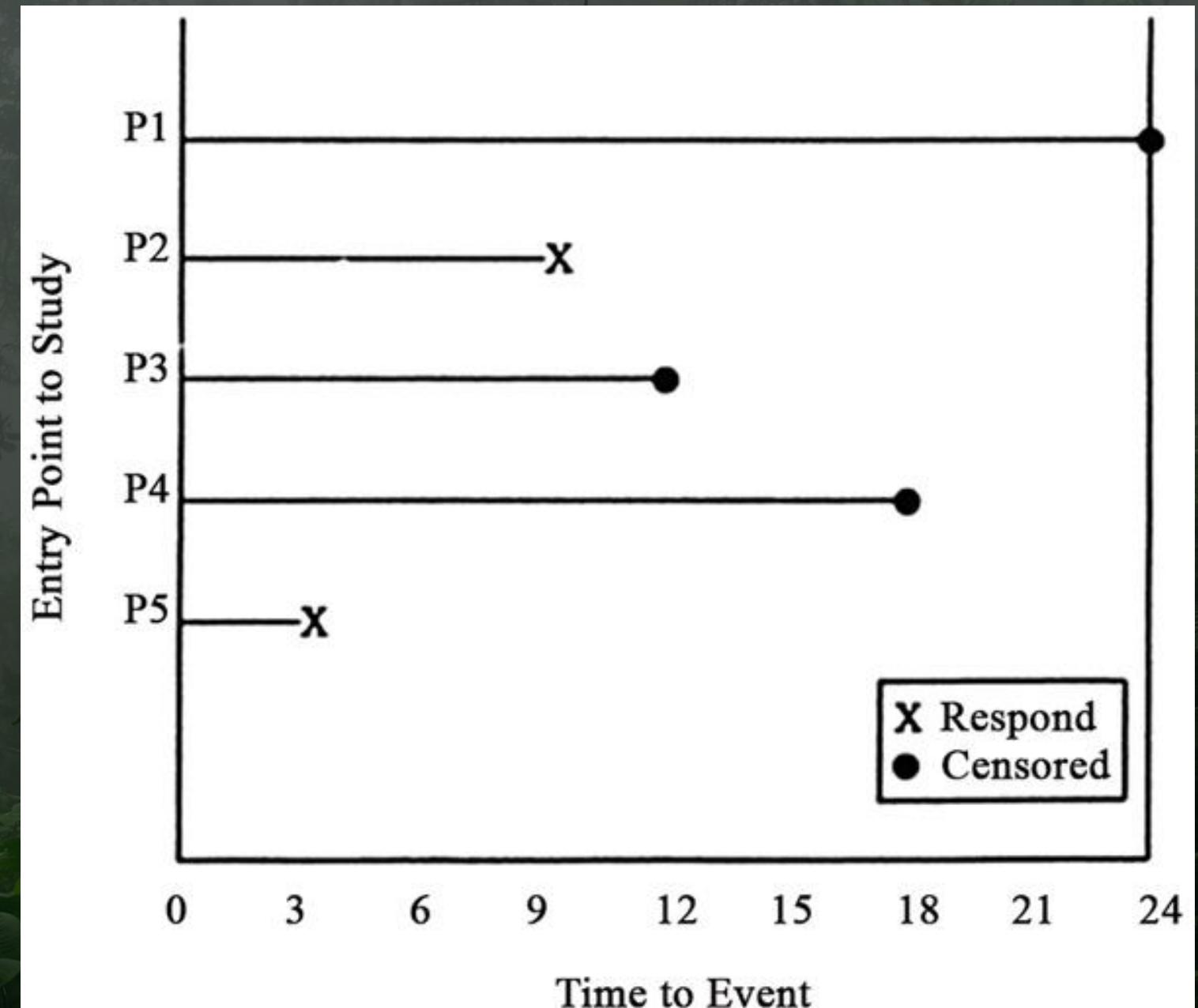
Data from 1974 to
present across 38
studies

*Fed only

≡ Results

Implementing Survival Models

- **Used to Estimate Time Until an Event Occurs**
 - Often applied in medicine/engineering
 - Event = a mosquito becoming infectious.
 - Median expected extrinsic incubation period (EIP) can be calculated from posterior predictions
- **Can handle right-censored data**
 - Classic statistical approaches (e.g., linear regression) don't account for censored data (mosquitoes that never become infectious within the study period).
 - Known as right-censoring



Parametric Survival Models

- For each disease, we analyzed 4 common time-to-event models: exponential, Weibull, gamma, and log-normal
- For each model, we incorporated a covariate for temperature (temp) to estimate the temperature sensitivity, viral load (clustered with k-means), and random effect (z) to account for between-study variation

Distribution	Model Equation	Parameters
Weibull	$T_i \sim \text{Weibull}(\lambda_i, k)$, $\log(\lambda_i) = \eta_i$	λ_i (scale), k (shape)
Exponential	$T_i \sim \text{Exponential}(\lambda_i)$, $\log(\lambda_i) = \eta_i$	λ_i (rate)
Gamma	$T_i \sim \text{Gamma}(\alpha, \beta_i)$, $\log(\beta_i) = \eta_i$	α (shape), β_i (rate)
Lognormal	$\log(T_i) \sim \mathcal{N}(\mu_i, \sigma)$, $\mu_i = \eta_i$	μ_i (mean), σ (SD)

Table 1. Parametric survival model formulations using different distributions.
The linear predictor is defined as:

$$\eta_i = \beta_0 + \beta_1 \cdot \text{temp}_i + \beta_2 \cdot \text{Mosquito.Species}_i + \beta_3 \cdot \text{cluster_vl}_i + (\text{random effects}).$$

Assumptions

Viral Load Assumptions

- TCID₅₀ approx. equivalent to CCID₅₀
- FFU approx. equivalent to PFU
- 1 PFU = 0.7 TCID₅₀ (accepted)
- A range of viral loads was set to the mean

General Assumptions

- Variance in degrees of less than 0.5 considered constant
- Days measured as a range set to mean
- Non-constant T values set as mean with DTR



Fine Tuning Models

Evaluation of Round 1 of Parametric Models

- Fit assessed with leave out one cross validation information criterion scores (LOOIC)
- Weibull best fit or tied for first and chosen for comparability across other disease areas.

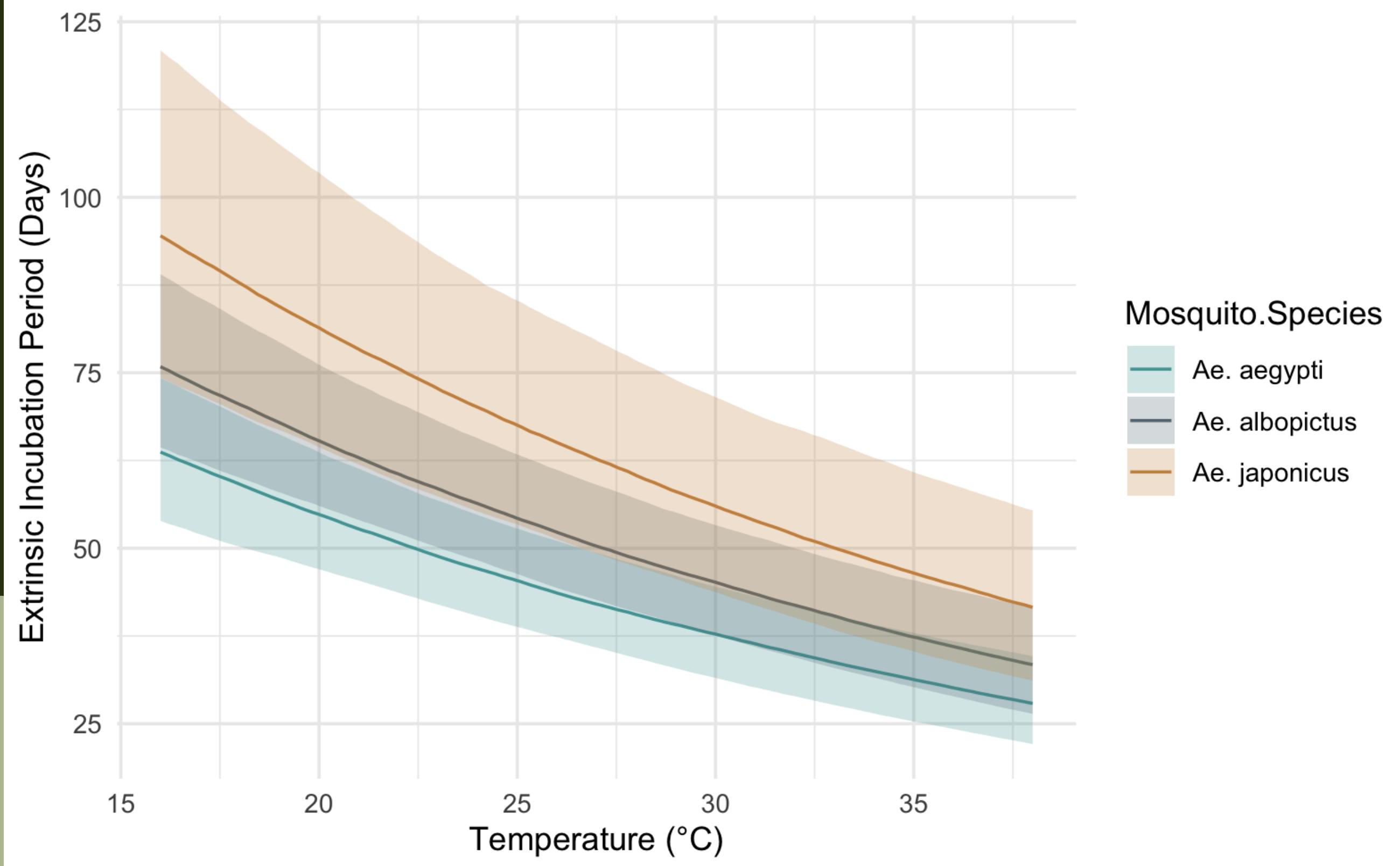
Fitting Weibull Models

- Further assessed:
 - Addition of: DTR, Mosquito Species, interactive effects, priors
 - Evaluated with LOOIC
- Each model's parameterization is*:
 - Disease specific based on data

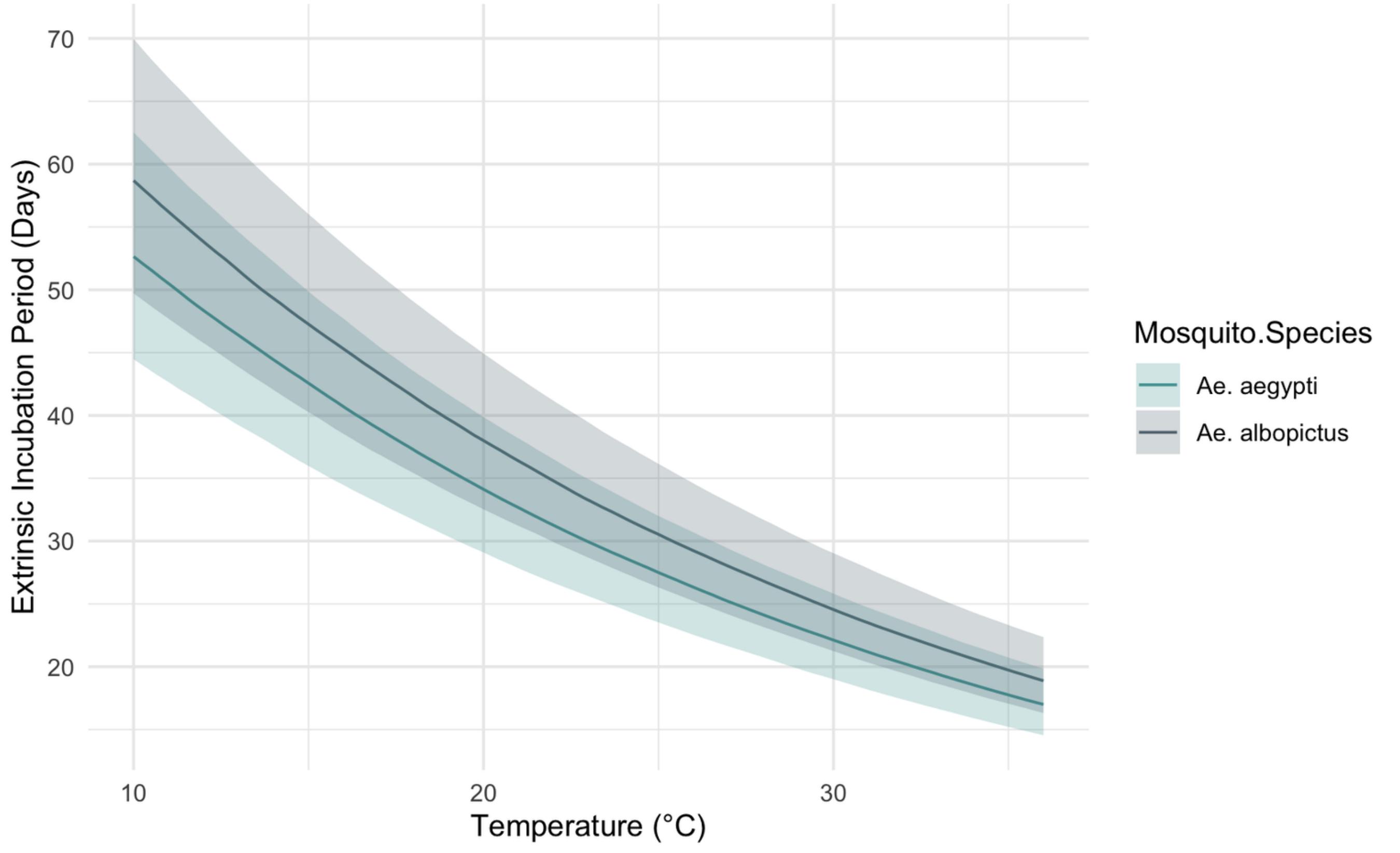
**when similar, chose model with least divergent transitions*

Zika Virus

Clear temperature dependence with variation by species



Dengue Virus



Greater overlap in species similarity compared to Zika

Limitations

- **Limited Experimental Data:**
 - Few studies have explicitly addressed the temperature dependence of the EIP for various arboviruses, leading to uncertainties in modeling disease transmission.
- **Variability in Experimental Approaches:**
 - Differences in mosquito populations, viral strains, and experimental conditions can lead to inconsistent EIP estimates.
- **Sensitivity to right-censored estimates:**
 - EIP10 vs EIP50 vs time to first event; priors

Future Directions

Next Steps

- Finalize Weibull models for all disease areas with estimates of EIP10/EIP50
- Compare viruses across the same vector species, where possible

Dataset to be open access with publication

Future Directions for Entomology

- Continue studies of vector competence for diseases and vectors at risk, especially in regions where burden is highest



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Thank You

For Your Attention

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