MODELING IN PRACTIVE: THE LIFE CYCLE OF A MODELING PROJECT, FROM CONCEPTION TO PUBLICATION

- The example of Buruli ulcer in Cameroon -

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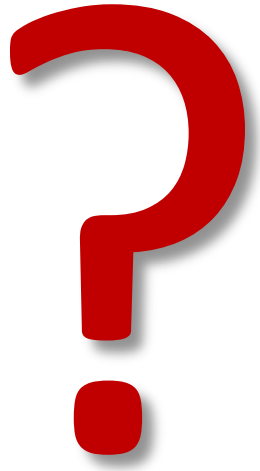
E²M² Workshop
Ranomafana, January 2020

Steps in a modeling project

1. *Development of the study concept and question*
2. *Literature review*
3. *Data collection*
4. *Construction of model framework*
5. *Model analyses and selection*
6. *Model validation*
7. *Manuscript writing and submission*

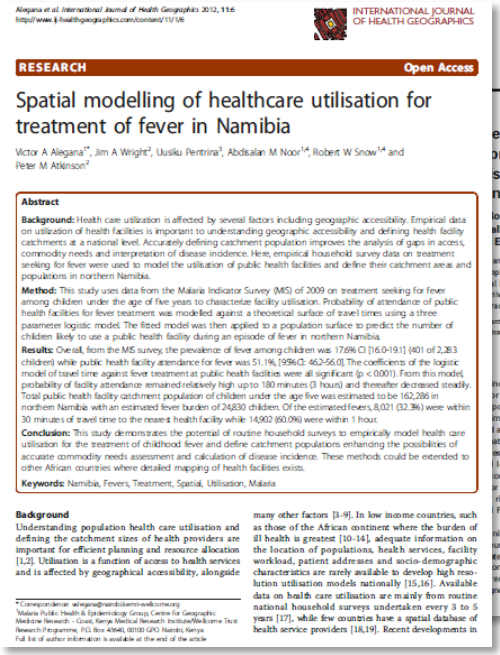
Development of the study concept



- What is your question?
- Why is it interesting?
- Who is interested?
- Can it be narrowed down to a question about specific quantitative relationships?

Literature review

- Who has tried to answer this before and how did they do it?
  - Empirical studies
  - Modeling studies
- What are these studies short-comings?
- Are there already parameter estimates or data sets to help you answer your question?


Alegana et al. International Journal of Health Geographics 2012, 11:6
http://www.ij-healthgeographics.com/content/11/1/6

INTERNATIONAL JOURNAL OF HEALTH GEOGRAPHICS

RESEARCH Open Access

Spatial modelling of healthcare utilisation for treatment of fever in Namibia

Victor A Alegana[1*], Jim A Wright[2], Uusiku Pentrina[3], Abdisalan M Noor[1,4], Robert W Snow[1,4] and Peter M Atkinson[2]

Abstract

Background: Health care utilisation is affected by several factors including geographic accessibility. Empirical data on utilisation of health facilities is important to understanding geographic accessibility and defining health facility catchments at a national level. Accurately defining catchment population improves the analysis of gaps in access, commodity needs and interpretation of disease incidence. Here, empirical household survey data on treatment seeking for fever were used to model the utilisation of public health facilities and define their catchment areas and populations in northern Namibia.

Method: This study uses data from the Malaria Indicator Survey (MIS) of 2009 on treatment seeking for fever among children under the age of five years to characterize facility utilisation. Probability of attendance of public health facilities for fever treatment was modelled against a theoretical surface of travel times using a three parameter logistic model. The fitted model was then applied to a population surface to predict the number of children likely to use a public health facility during an episode of fever in northern Namibia.

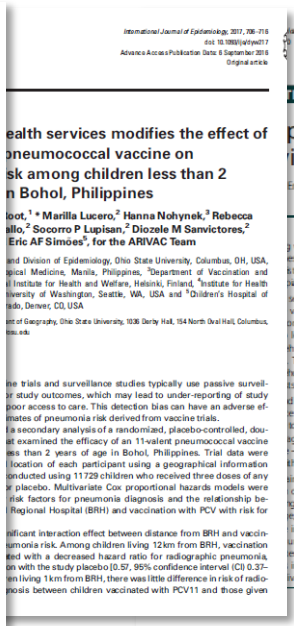
Results: Overall, from the MIS survey, the prevalence of fever among children was 17.6% CI [16.0-19.1] (401 of 2,283 children) while public health facility attendance for fever was 51.1%, [95% CI: 46.2-56.0]. The coefficients of the logistic model of travel time against fever treatment at public health facilities were all significant ($p < 0.001$). From this model, probability of facility attendance remained relatively high up to 100 minutes (1 hours) and thereafter decreased steadily. Total public health facility catchment population of children under the age five was estimated to be 162,286 in northern Namibia with an estimated fever burden of 24,830 children. Of the estimated fevers, 8,021 (32.3%) were within 30 minutes of travel time to the nearest health facility while 14,902 (60.0%) were within 1 hour.

Conclusion: This study demonstrates the potential of routine household surveys to empirically model health care utilisation for the treatment of childhood fever and define catchment populations enhancing the possibilities of accurate commodity needs assessment and calculation of disease incidence. These methods could be extended to other African countries where detailed mapping of health facilities exists.

Keywords: Namibia, Fevers, Treatment, Spatial, Utilisation, Malaria

Background

Understanding population health care utilisation and defining the catchment sizes of health providers are important for efficient planning and resource allocation [1,2]. Utilisation is a function of access to health services and is affected by geographical accessibility, alongside many other factors [3-9]. In low income countries, such as those of the African continent where the burden of ill health is greatest [10-14], adequate information on the location of populations, health services, facility workload, patient addresses and socio-demographic characteristics are rarely available to develop high resolution utilisation models nationally [15,16]. Available data on health care utilisation are mainly from routine national household surveys undertaken every 3 to 5 years [17], while few countries have a spatial database of health service providers [18,19]. Recent developments in


International Journal of Epidemiology, 2017, 706–716
doi: 10.1093/ije/yw017
Advance Access Publication Date: 8 September 2016
Original article

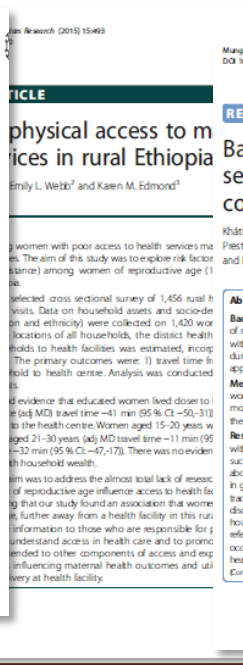
ealth services modifies the effect of pneumococcal vaccine on sk among children less than 2 n Bohol, Philippines

oot,[1] * Marilla Lucero,[2] Hanna Nohynek,[3] Rebecca llo,[2] Socorro P Lupisan,[2] Diozele M Sanvictores,[2] Eric AF Simões[5], for the ARIVAC Team

nd Division of Epidemiology, Ohio State University, Columbus, OH, USA, pical Medicine, Manila, Philippines, [3]Department of Vaccination and l Institute for Health and Welfare, Helsinki, Finland, [4]Institute for Health versity of Washington, Seattle, WA, USA and [5]Children's Hospital of ado, Denver, CO, USA

ne trials and surveillance studies typically use passive surveilr study outcomes, which may lead to under-reporting of study poor access to care. This detection bias can have an adverse efmates of pneumonia risk derived from vaccine trials.
a secondary analysis of a randomized, placebo-controlled, doubt examined the efficacy of an 11-valent pneumococcal vaccine onducted using 11729 children who received three doses of any r placebo. Multivariate Cox proportional hazards models were risk factors for pneumonia diagnosis and the relationship be-Regional Hospital (BRH) and vaccination with PCV with risk for

nificant interaction effect between distance from BRH and vaccinumonia risk. Among children living 12km from BRH, vaccination ted with a decreased hazard ratio for radiographic pneumonia, on with the study placebo [0.57, 95% confidence interval (CI) 0.37en living 1km from BRH, there was little difference in risk of radionosis between children vaccinated with PCV11 and those given


Munguambe et al. Reproductive Health 2016, 13(Suppl 1):31
DOI 10.1186/s12978-016-0141-0

RESEARCH

hysical access to m ices in rural Ethiopia

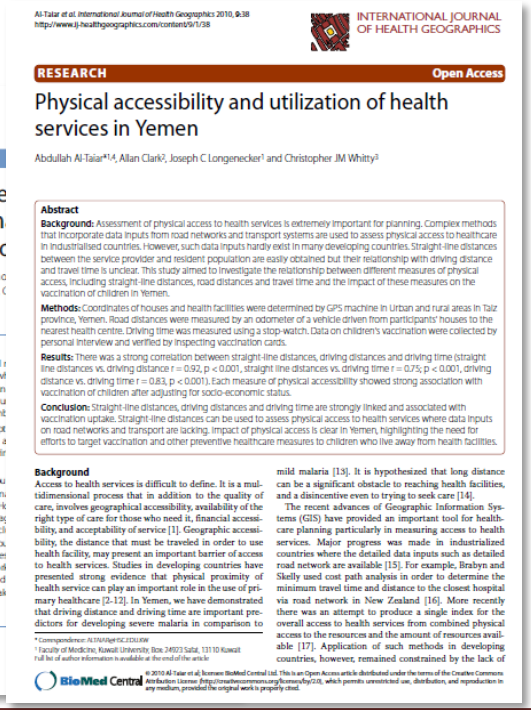
Emily L. Webb[2] and Karen M. Edmond[1]

women with poor access to health services ma
The aim of this study was to explore risk factor
stance) among women of reproductive age (1

elected cross sectional survey of 1,456 rural h
visits. Data on household assets and socio-de
on and ethnicity) were collected on 1,420 wor
locations of all households, the district health
holds to health facilities was estimated, incorp
The primary outcomes were: 1) travel time fr
hold to health centre. Analysis was conducted

d evidence that educated women lived closer to
e (adj MD) travel time −41 min (95 % CI: −50,-31)]
to the health centre. Women aged 15–20 years w
ged 21–30 years (adj MD travel time −11 min (95
−32 min (95 % CI: −47,-17)). There was no eviden
h household wealth.

im was to address the almost total lack of researc
of reproductive age influence access to health fa
g that our study found an association that wome
e, further away from a health facility in this rur
information to those who are responsible for
understand access in health care and to promo
ended to other components of access and equ
influencing maternal health outcomes and uti
very at health facility.


Al-Taiar et al. International Journal of Health Geographics 2010, 9:38
http://www.ij-healthgeographics.com/content/9/1/38

INTERNATIONAL JOURNAL OF HEALTH GEOGRAPHICS

RESEARCH Open Access

Physical accessibility and utilization of health services in Yemen

Abdullah Al-Taiar[*1,4], Allan Clark[2], Joseph C Longenecker[1] and Christopher JM Whitty[3]

Abstract

Background: Assessment of physical access to health services is extremely important for planning. Complex methods that incorporate data inputs from road networks and transport systems are used to assess physical access to healthcare in industrialised countries. However, such data inputs hardly exist in many developing countries. Straight-line distances between the service provider and resident population are easily obtained but their relationship with driving distance and travel time is unclear. This study aimed to investigate the relationship between different measures of physical access, including straight-line distances, road distances and travel time and the impact of these measures on the vaccination of children in Yemen.

Methods: Coordinates of houses and health facilities were determined by GPS machine in Urban and rural areas in Taiz province, Yemen. Road distances were measured by an odometer of a vehicle driven from participants' houses to the nearest health centre. Driving time was measured using a stop-watch. Data on children's vaccination were collected by personal interview and verified by inspecting vaccination cards.

Results: There was a strong correlation between straight-line distances, driving distances and driving time (straight line distances vs. driving distance $r = 0.92$, $p < 0.001$, straight line distances vs. driving time $r = 0.75$; $p < 0.001$, driving distance vs. driving time $r = 0.83$, $p < 0.001$). Each measure of physical accessibility showed strong association with vaccination of children after adjusting for socio-economic status.

Conclusion: Straight-line distances, driving distances and driving time are strongly linked and associated with vaccination uptake. Straight-line distances can be used to assess physical access to health services where data inputs on road networks and transport are lacking. Impact of physical access is clear in Yemen, highlighting the need for efforts to target vaccination and other preventive healthcare measures to children who live away from health facilities.

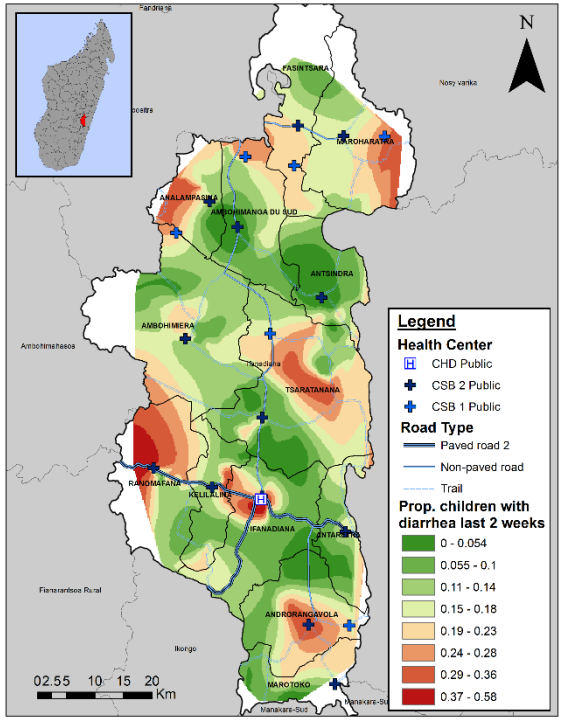
Background

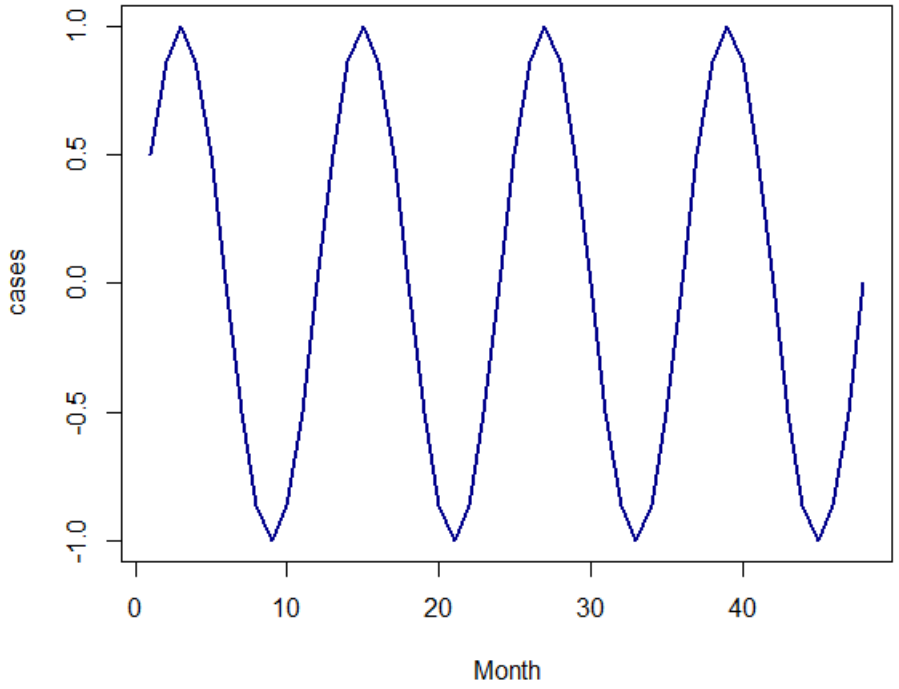
Access to health services is difficult to define. It is a multidimensional process that in addition to the quality of care, involves geographical accessibility, availability of the right type of care for those who need it, financial accessibility, and acceptability of service [1]. Geographic accessibility, the distance that must be traveled in order to use health facility, may present an important barrier of access to health services. Studies in developing countries have presented strong evidence that physical proximity of health service can play an important role in the use of primary healthcare [2-12]. In Yemen, we have demonstrated that driving distance and driving time are important predictors for developing severe malaria in comparison to mild malaria [13]. It is hypothesized that long distance can be a significant obstacle to reaching health facilities, and a disincentive even to trying to seek care [14].

The recent advances of Geographic Information Systems (GIS) have provided an important tool for healthcare planning particularly in measuring access to health services. Major progress was made in industrialized countries where the detailed data inputs such as detailed road network are available [15]. For example, Brabyn and Skelly used cost path analysis in order to determine the minimum travel time and distance to the closest hospital via road network in New Zealand [16]. More recently there was an attempt to produce a single index for the overall access to health services from combined physical access to the resources and the amount of resources available [17]. Application of such methods in developing countries, however, remained constrained by the lack of

Data collection

- What do you need to characterize?
  - Spatial and/or temporal dynamics
  - Relationships between parameters or systems



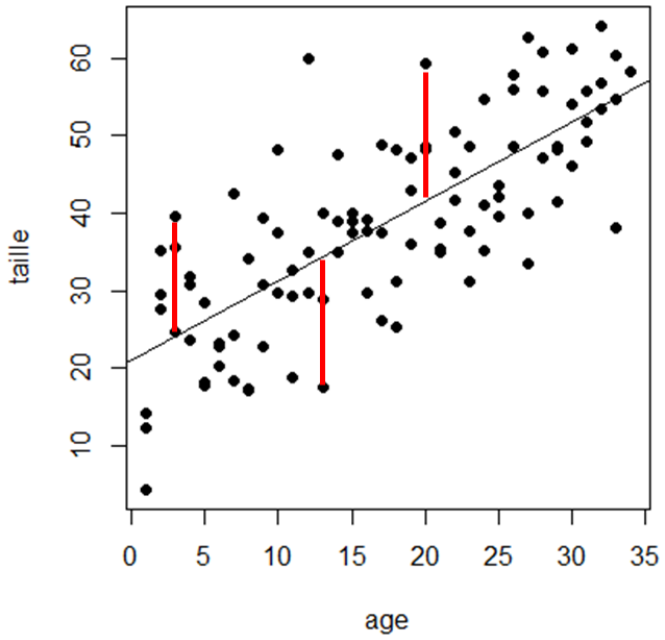


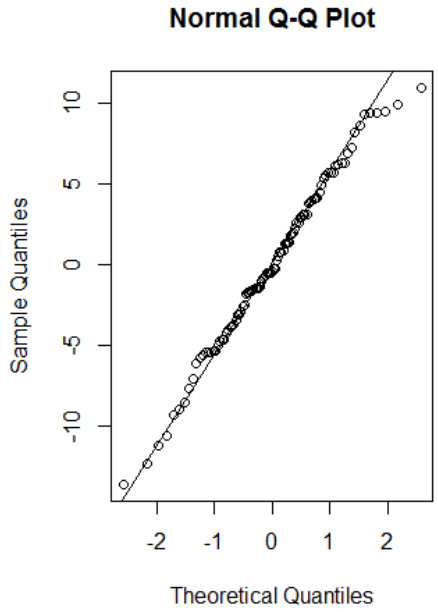
Construction of model framework

- What drawbacks of previous studies can I mitigate?
- What type of modeling is necessary to answer my question?
  - Statistical: GLM, spatial, time-series, etc.
  - Mathematical: population based, individual based
- What modeling elements are necessary for my question?
  - Stochasticity
  - Compartments and complexity

Model analysis, selection and validation

- What model(s) best fit my data and explain my question?
  - Comparison of alternative models and application of selection procedures
- Does the selected model suffer from any substantial drawbacks?
  - Statistical models: verification of model assumptions
  - Mathematical models: sensitivity analyses and out-of-sample predictions





Types of modeling studies

Without data collection

1. Purely theoretical studies
2. Parametrization based on published studies
   - Systematic reviews and meta-analyses
   - Experimental and field studies

1. Development of the study concept
2. Literature Review
3. Data collection
4. Construction of model framework
   - Dynamic equations and code
   - Relationships between parameters
5. Model analyses and selection
   - Parametrization
   - Simulations and debugging
6. Model validation
   - Model validation
   - Sensitivity analyses
7. Manuscript writing and submission

Types of modeling studies

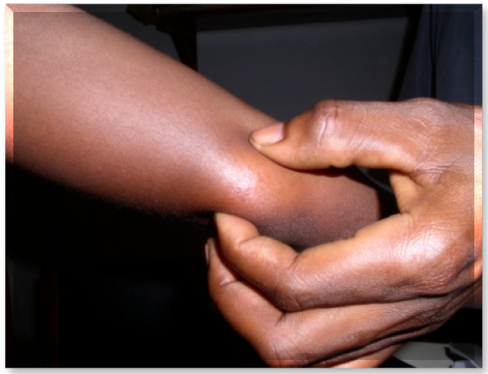
1. Development of the study concept
2. Literature Review
3. **Data collection**
4. Construction of model framework
   - Statistical vs. Mathematical model
   - Model better adapted to our data
5. Model analyses and selection
   - Descriptive, univariate and multivariate
   - Parametrization and simulations
6. Model validation
   - Model validation, comparison
   - Sensitivity analyses
7. Manuscript writing and submission

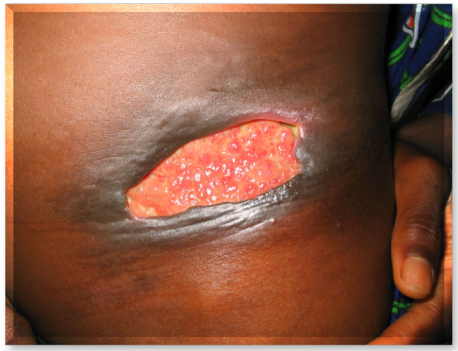
With data collection

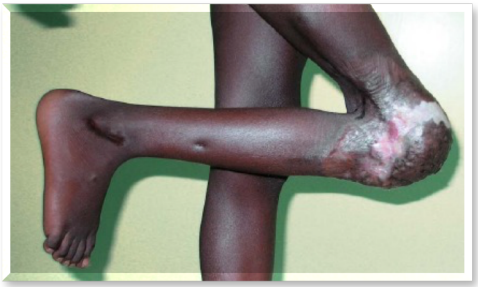
1. Data already collected for other purposes
   - Focus only on analyses
   - Need to understand data limitations and quality
   - Need to adapt modeling to the available data
2. Data collected for the modeling project
   - Very time consuming
   - Modeling is generally more straightforward

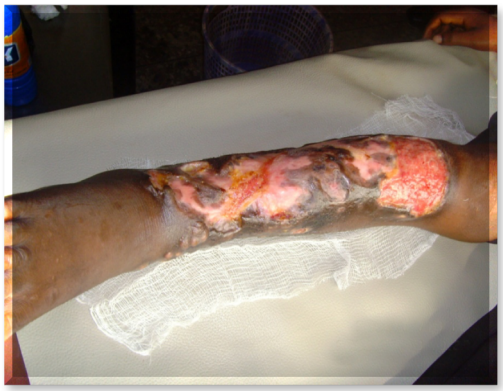
THE EXAMPLE OF BURULI ULCER IN CAMEROON

Buruli ulcer

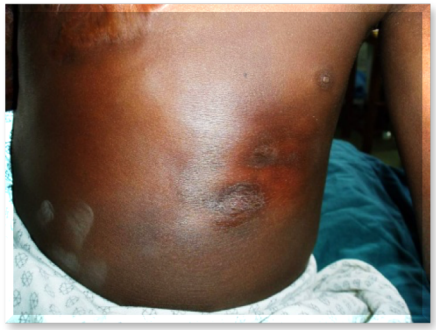




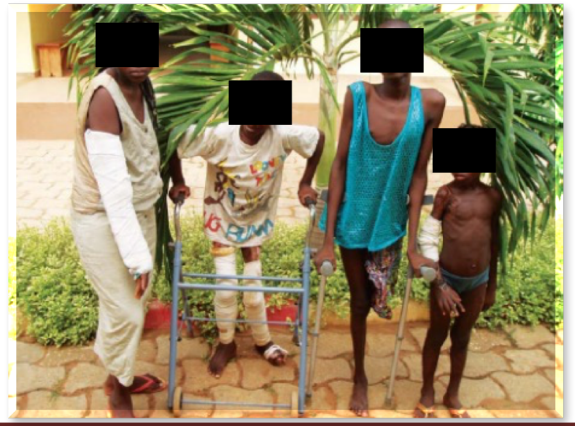




Most affected : Children <15 years

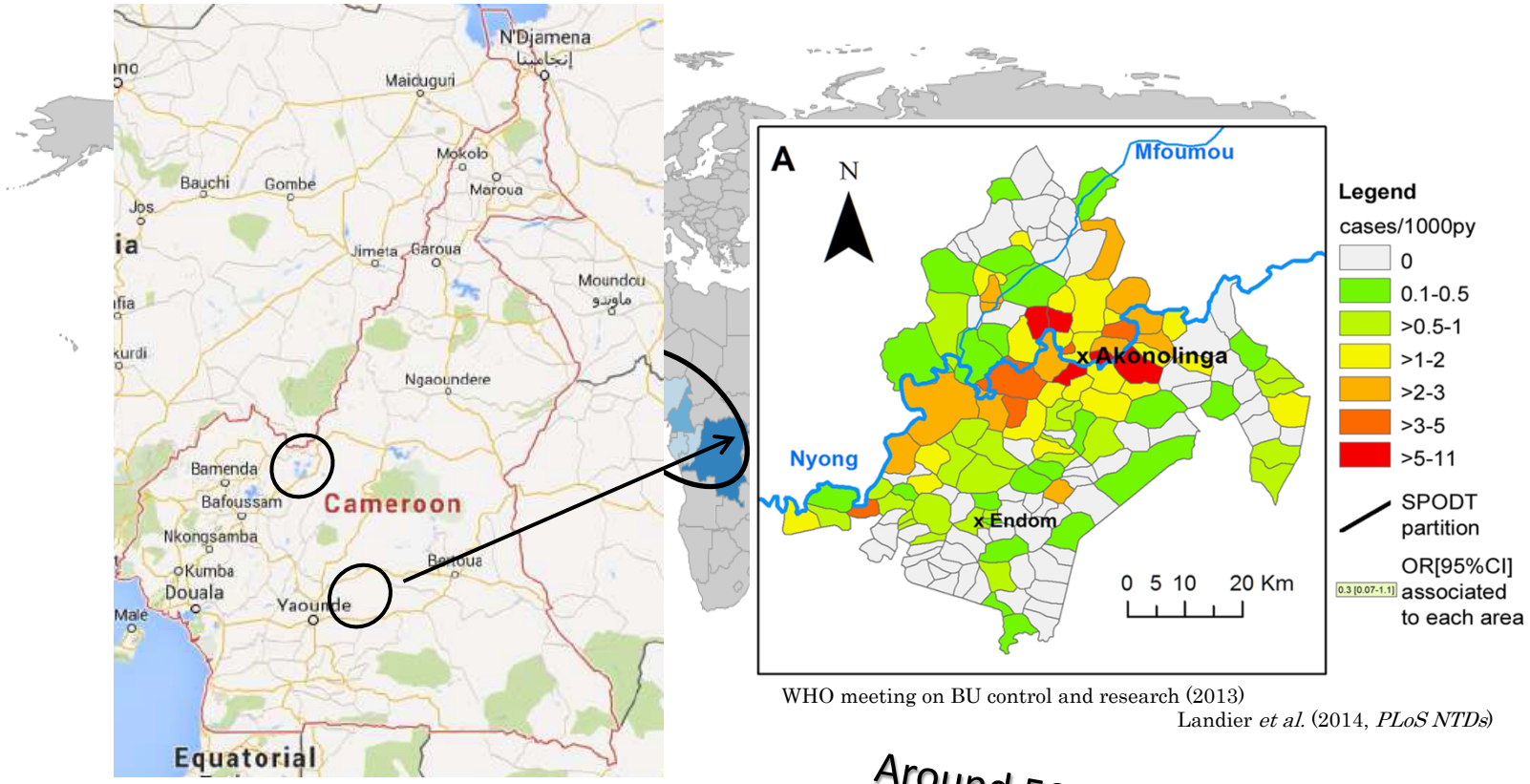


25% cases with functional limitations



Source of images: www.who.int (2014)

Buruli ulcer: an emergent and neglected disease



WHO meeting on BU control and research (2013)

Landier *et al.* (2014, *PLoS NTDs*)

Cases in more than 30 countries

Focal distribution

Around 5000 new cases each year

What is my question?

Why is it interesting?

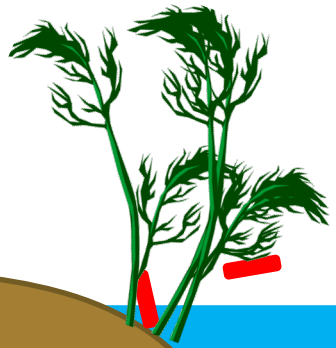
Who has tried to answer this before and how?

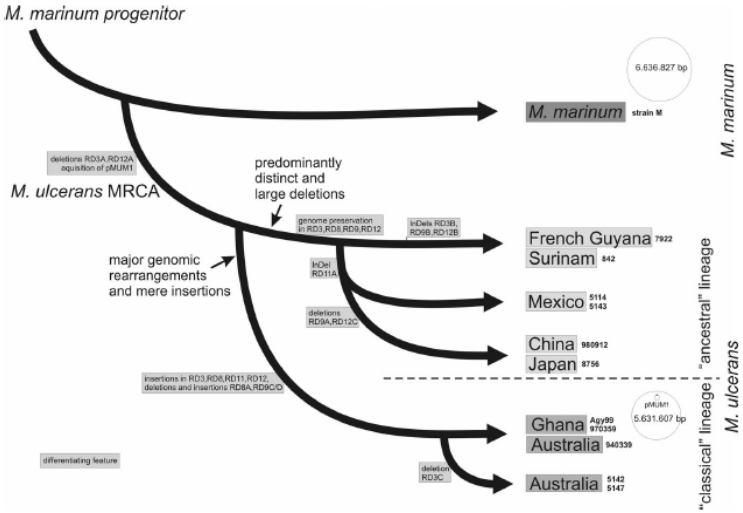
What are these studies short-comings?

1. LITERATURE REVIEW
&
IDENTIFICATION OF THE PROBLEM

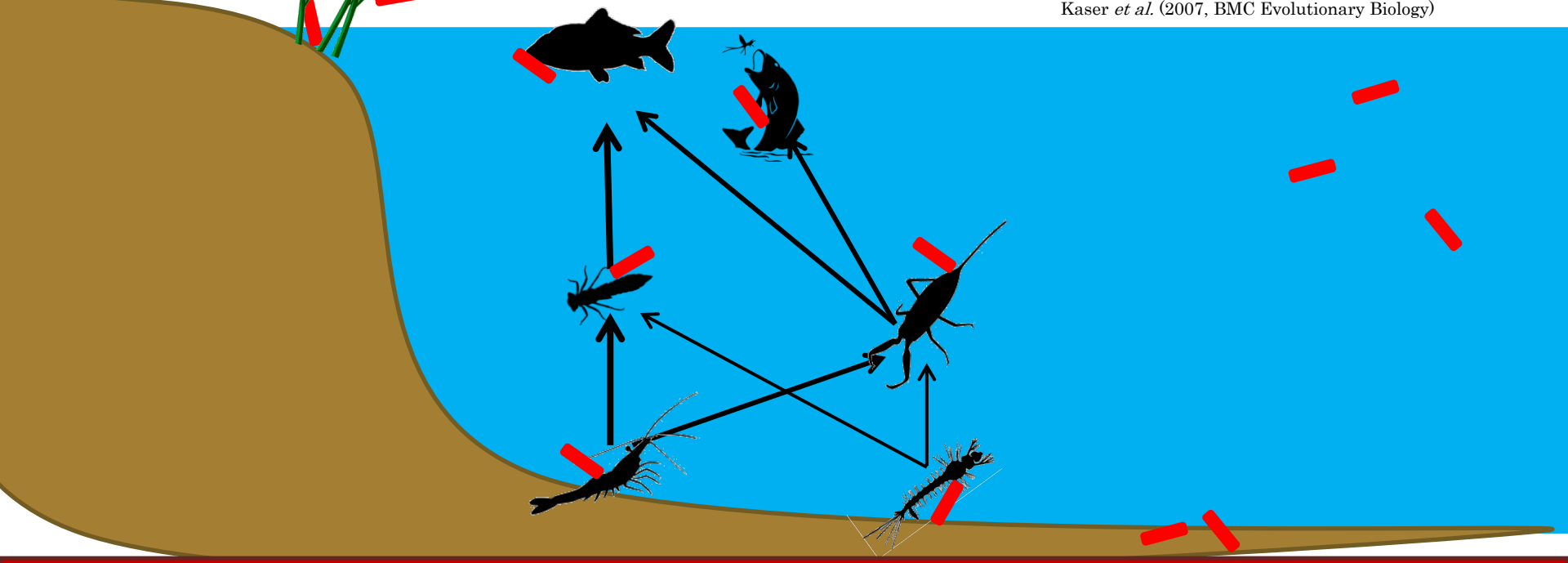
Mycobacterium ulcerans: generalities

Multi-host
&
Environmentally persistent





Kaser *et al.* (2007, BMC Evolutionary Biology)



Buruli ulcer: a disease linked to aquatic ecosystems

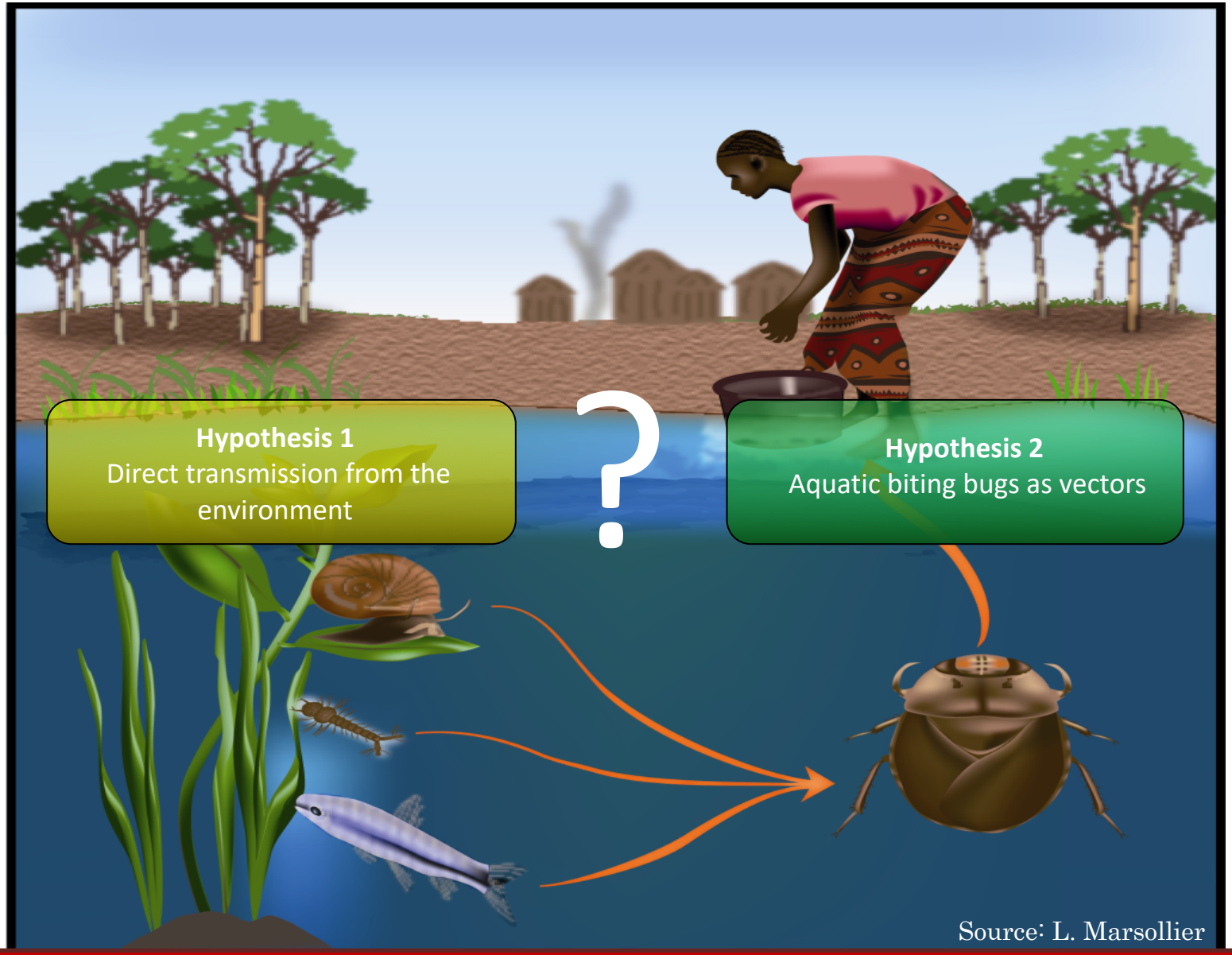
BU Risk factors

Proximity to stagnant or slow flowing waters

Activities near water

M. ulcerans

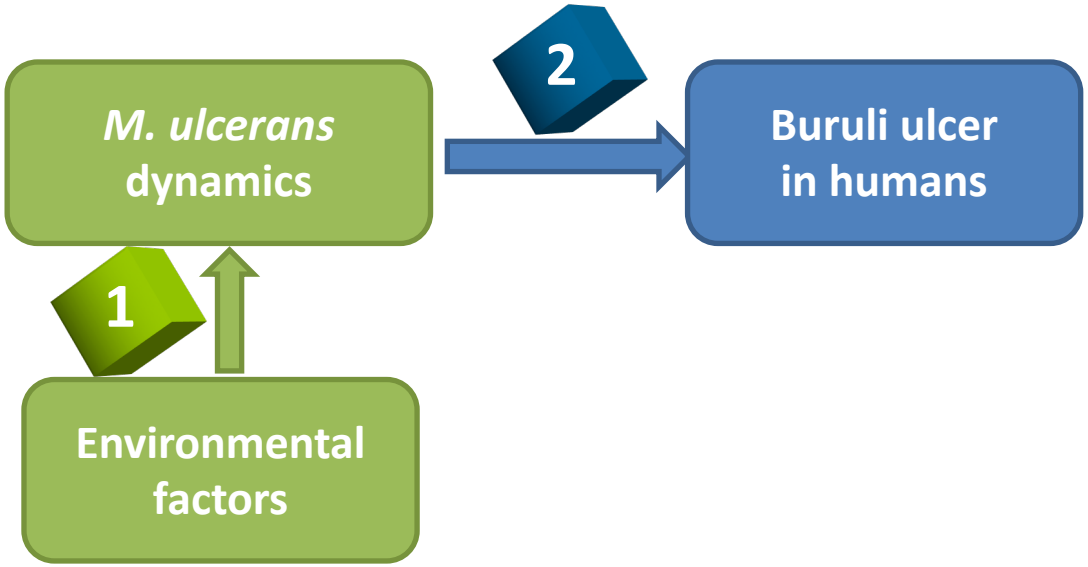
Buruli ulcer: a mysterious disease



iii Objectives of the project

General objective

To gain insights on the ecological determinants of Buruli ulcer disease.



Specific objectives

1. To understand the effects of environmental factors on *M.ulcerans* ecology
2. To study the transmission of *M.ulcerans* from the aquatic environment to humans

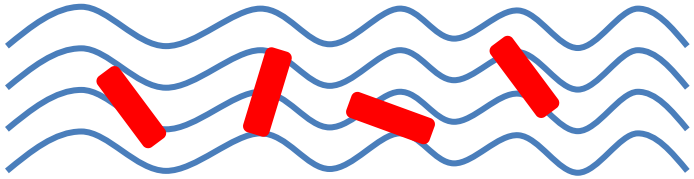
What do I need to characterize?

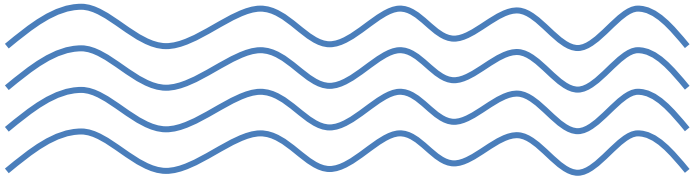
Spatial and/or temporal dynamics?

Relationships between parameters or systems?

DATA COLLECTION & DESCRIPTIVE ANALYSES

1 Introduction





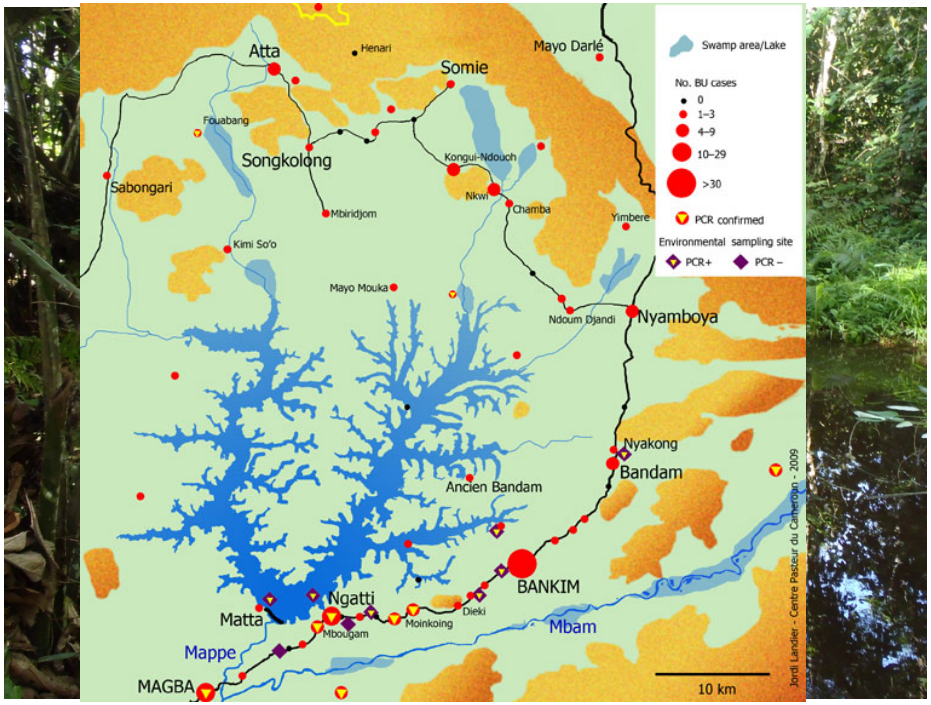
1 Regions of study

Akonolinga

- Landscape: Tropical rainforest
- Historically endemic area (>40 years)

Bankim

- Landscape: Savannah-Forest
- New endemic area (10 years)



Marion *et al.* (2011, *EID*)

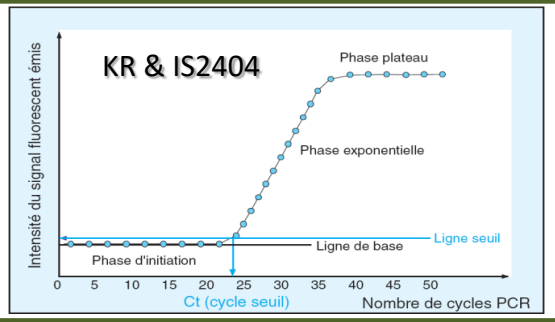
Landier *et al.* (2014, *PLoS NTDs*)

Characterization of MU in the environment

1. Fieldwork: Environmental sampling

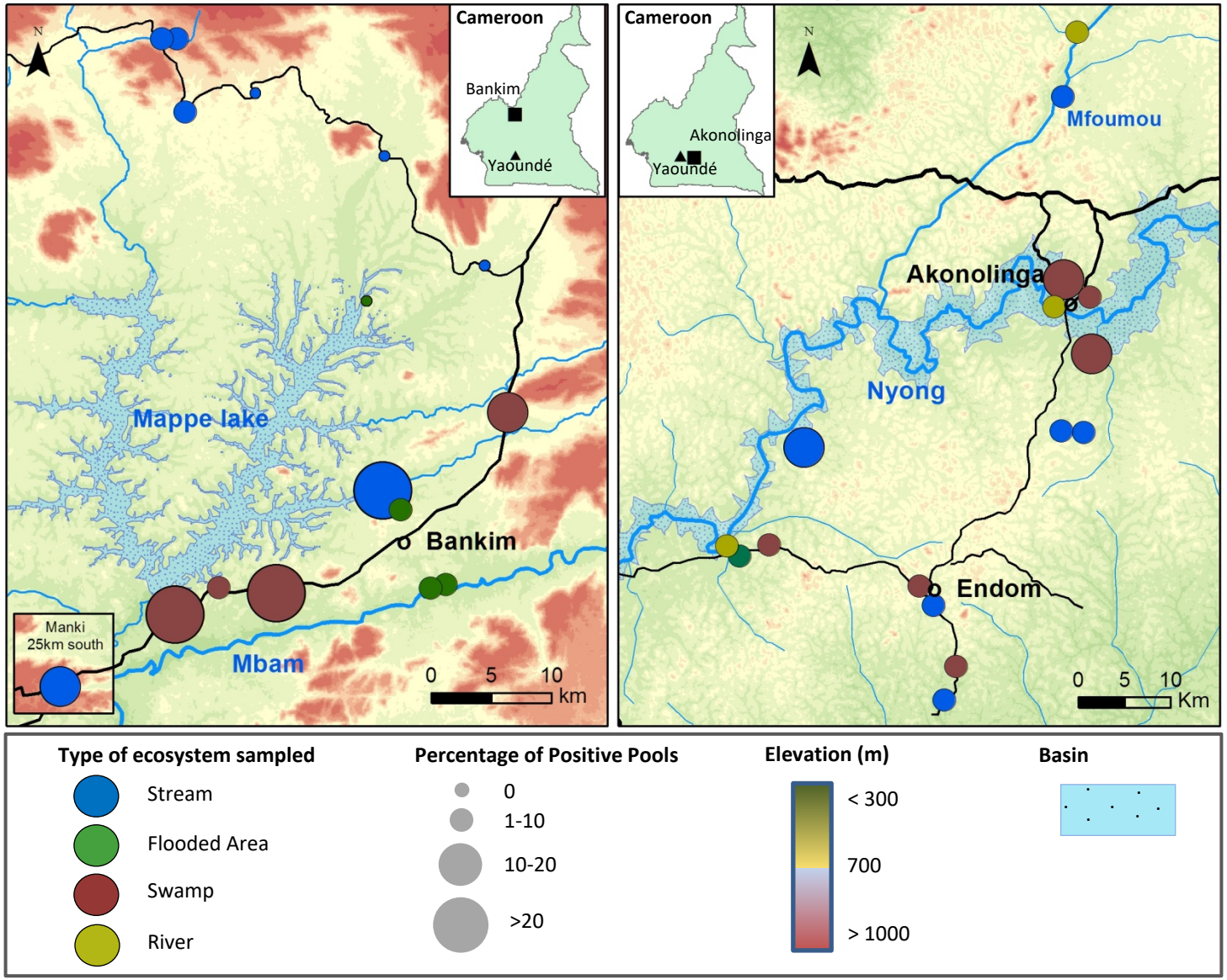
2. Laboratory (CPC): Taxonomic identification & Pool composition

3. Laboratory (Angers): DNA extraction & Amplification



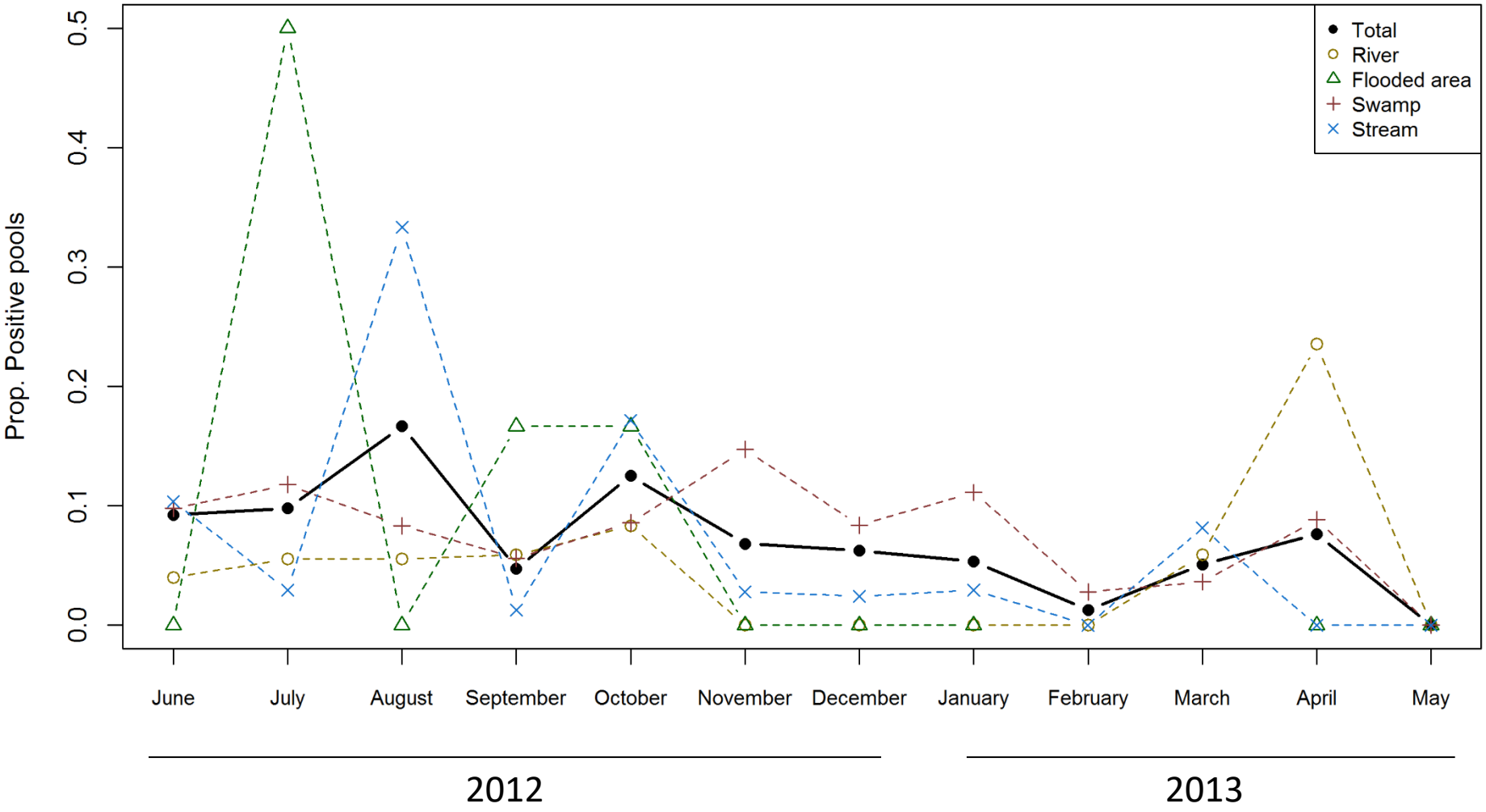
Characterization of MU in the environment

1 *M. ulcerans* geographical distribution



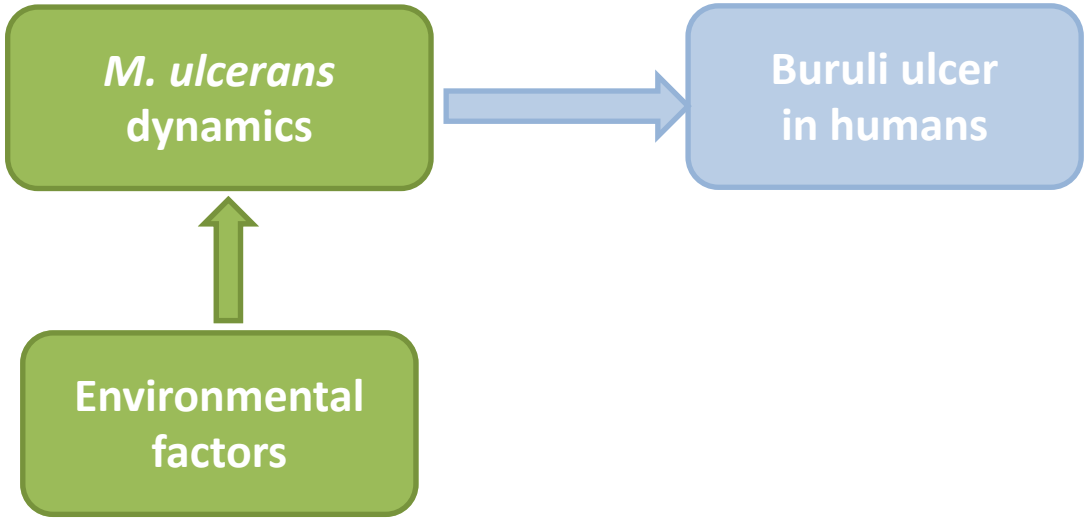
Garchitorena *et al.* (2014, *PloS NTDs*)

1 Seasonal fluctuations of *M. ulcerans in* freshwater ecosystems



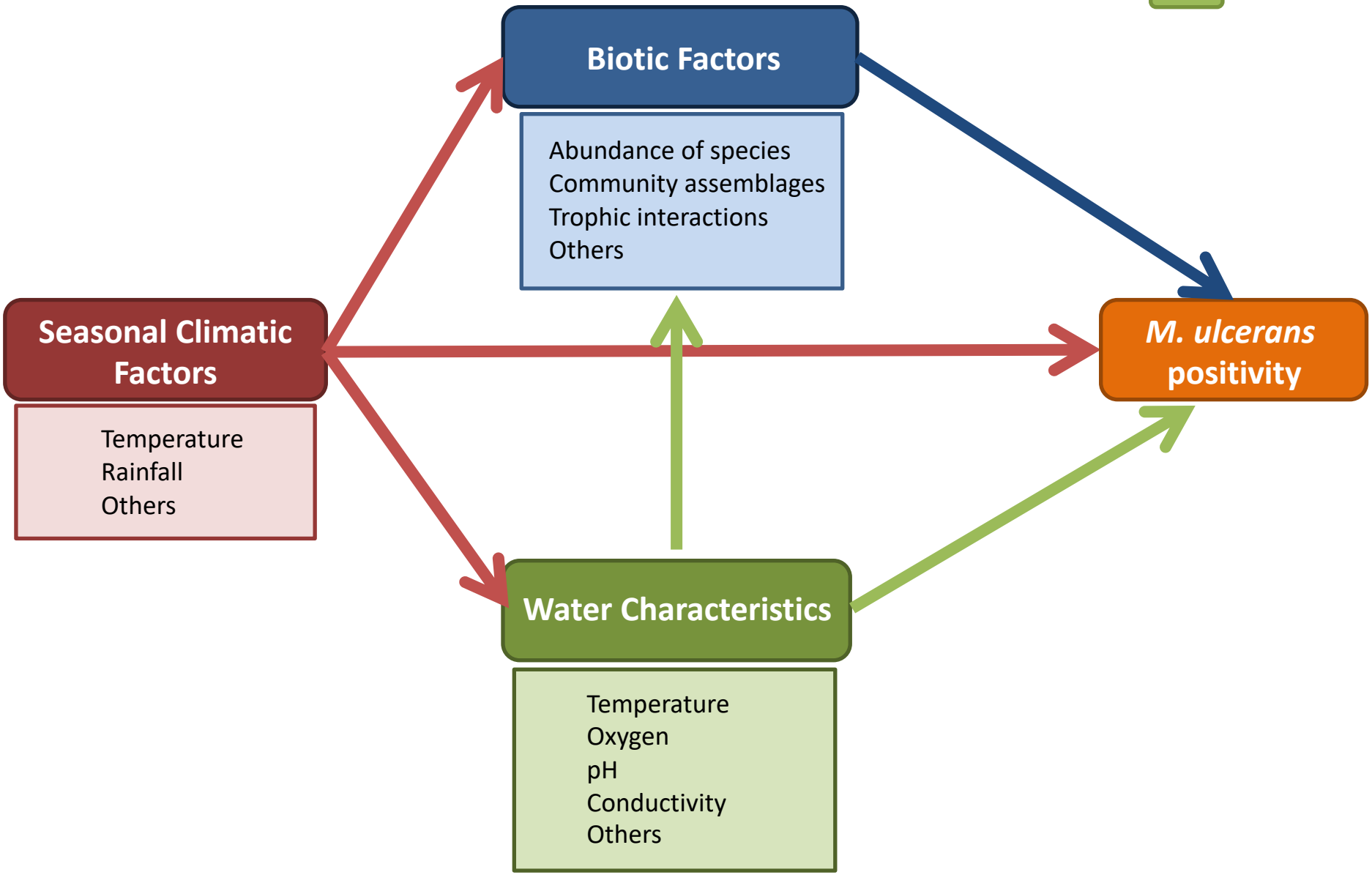
Garchitorena *et al.* (2014, *PloS NTDs*)

What type of modeling is necessary to answer my question?



STATISTICAL ANALYSES TO UNDERSTAND M. ULCERANS ECOLOGY

2 Environmental drivers of *M. ulcerans*



2 Methodology: Multi-model approach

Model Definition

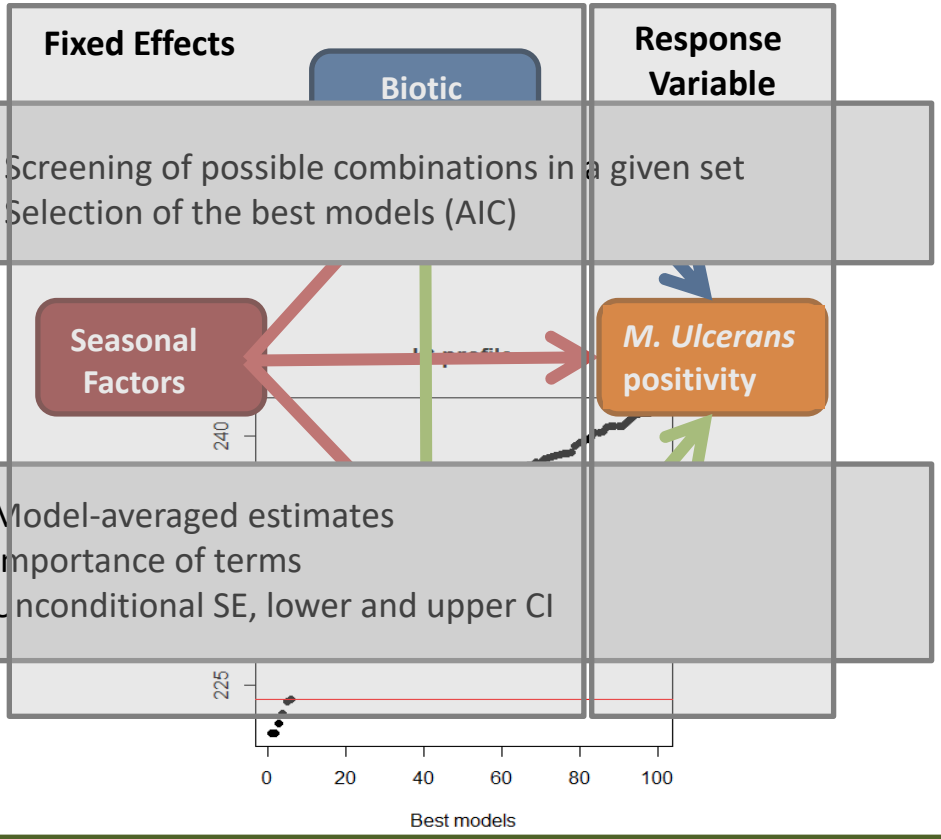
- Generalized linear mixed model (binomial)
- **Random effect**: Sample site

Multi-model Selection

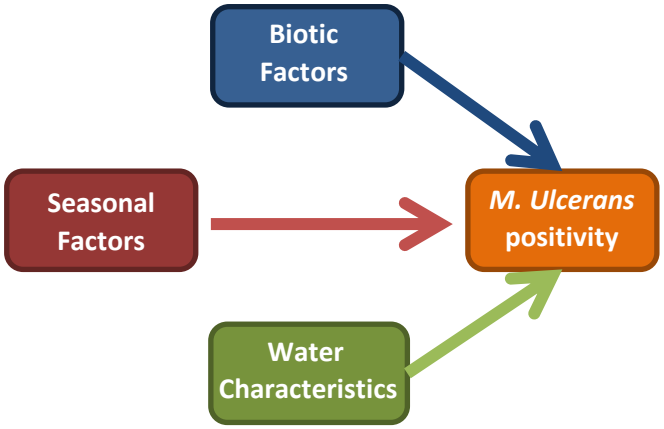
- Screening of possible combinations in a given set
- Selection of the best models (AIC)

Multi-model Inference

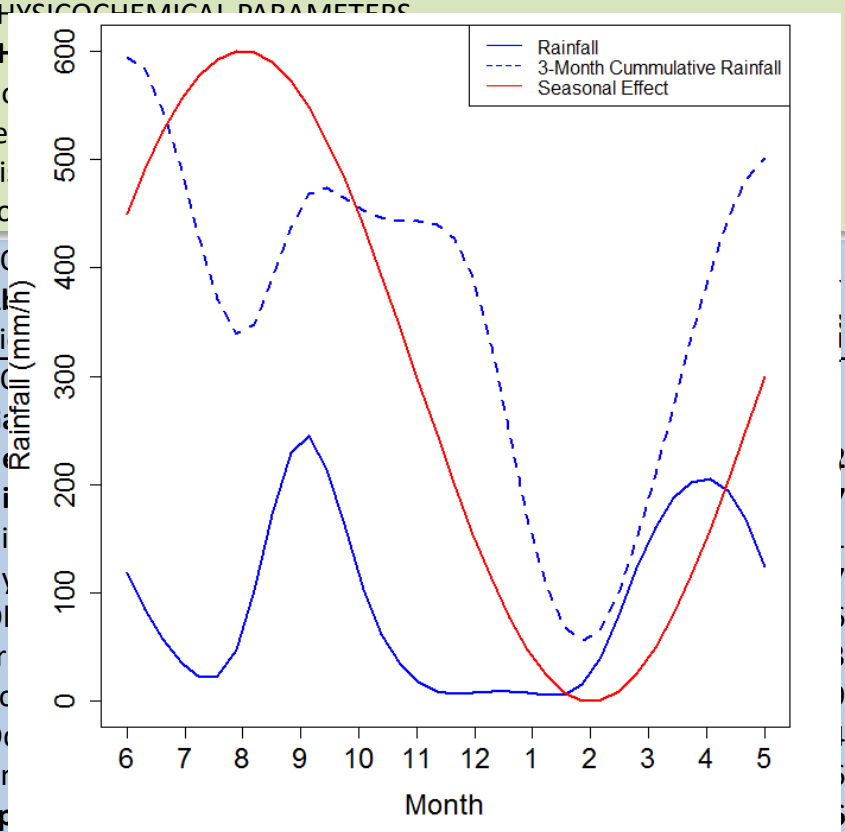
- Model-averaged estimates
- Importance of terms
- Unconditional SE, lower and upper CI



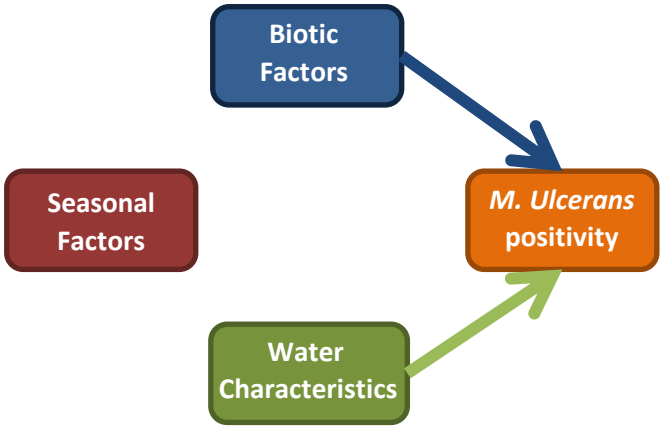
2 Environmental drivers of *M. ulcerans:* Akonolinga



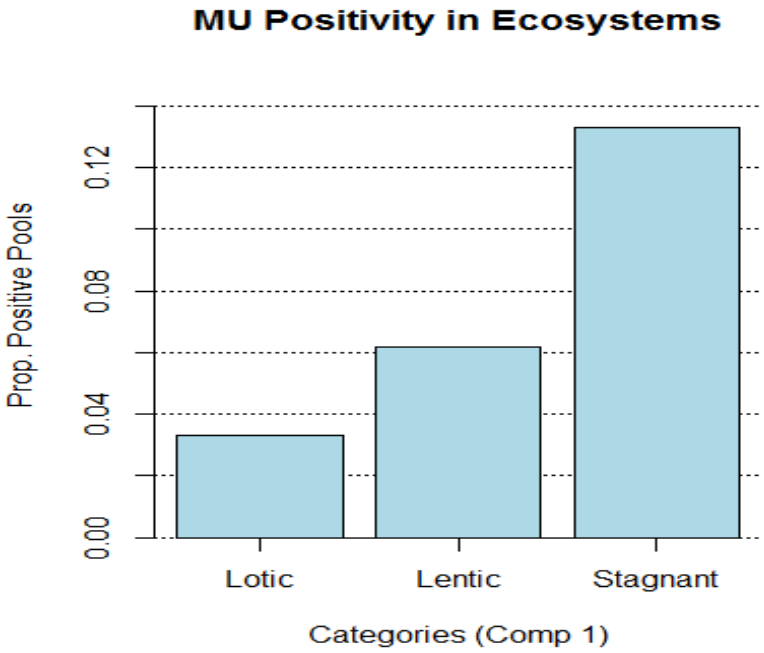
Variable	Avg.beta	Lower.CL	Upper.CL	Relative Importance
(Intercept)	**-13,66**	**-22,50**	**-4,82**	**1**
SEASONALITY				
Sin(2pi*Mois/12)	**0,35**	**0,02**	**0,69**	**1**
Sin(2pi*Mois/4)				
Cos(2pi*Mois/12)				
Cos(2pi*Mois/4)				
PHYSICOCHEMICAL PARAMETERS				
pH				
Fl				
Te				
Di				
Co				
AQ				
Al				
Bi				
AQ				
Ga				
He				
Hi				
Di				
Hy				
Ol				
Tr				
Co				
Oc				
An				
Ep				
Decapoda	**-1,01**	**-1,81**	**-0,21**	**0,21**

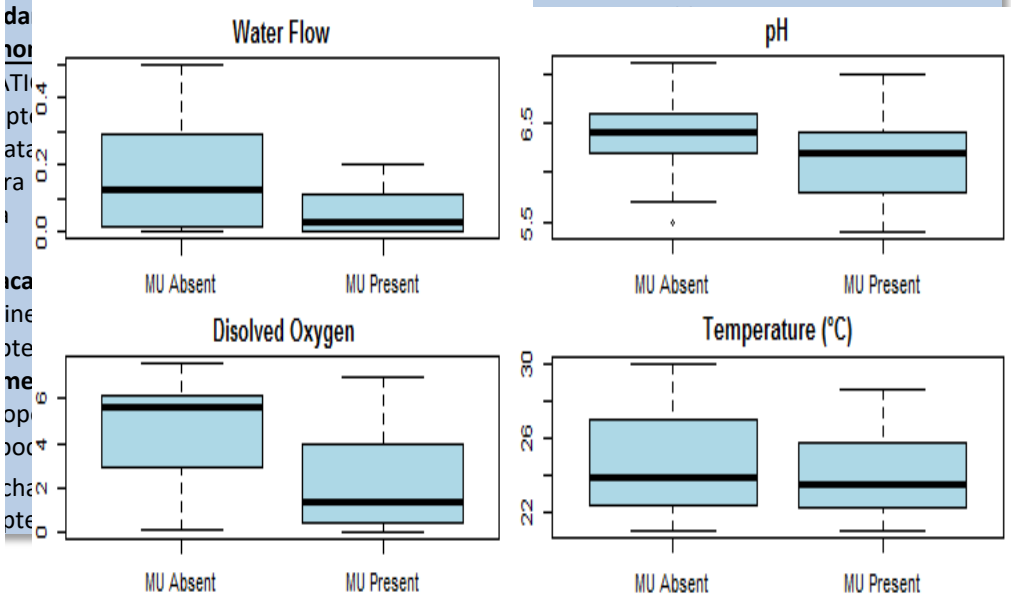


2 Environmental drivers of *M. ulcerans:* Bankim

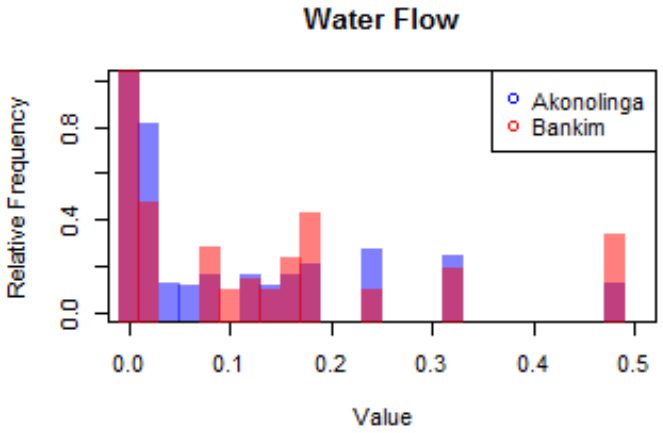


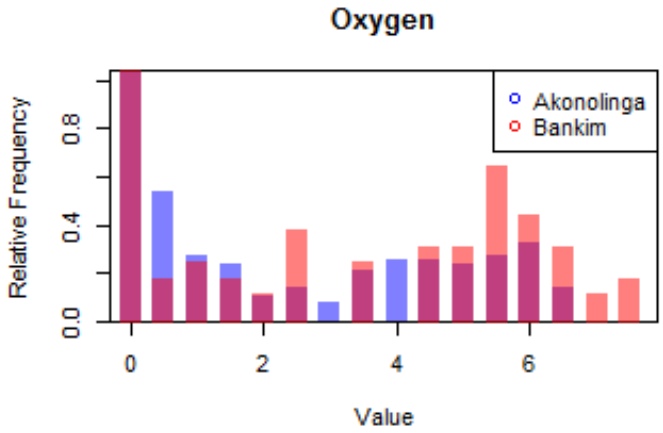
Variable	Avg.beta	Lower.CL	Upper.CL	Relative.Importance
(Intercept)	**-10,13**	**-18,94**	**-1,32**	**1**
PHYSICO-CHEMICAL PARAMETERS				
Water Flow (lentic)	**-1,91**	**-3,25**	**-0,57**	**1**
Water Flow (lotic)	**-2,86**	**-4,38**	**-1,33**	**1**
pH	-5,52	-15,64	4,61	0,02
Temperature				
Dissolved Oxygen				
Conductivity				
Comp3	0,24	-0,57	1,06	0,05
Comp1	0,34	-0,24	0,92	0,02
Comp2	-0,16	-0,85	0,53	0,01
COMMUNITY				

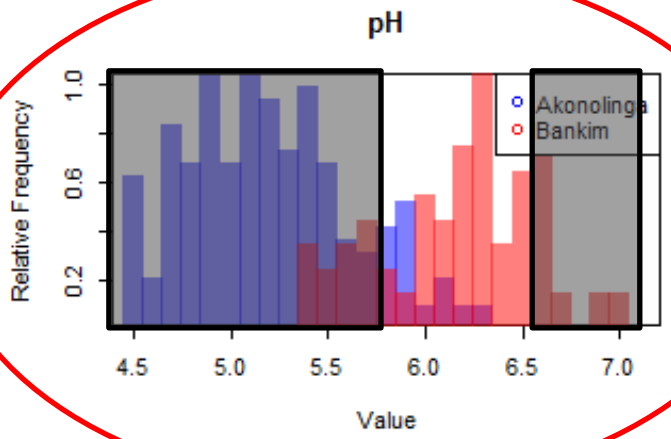


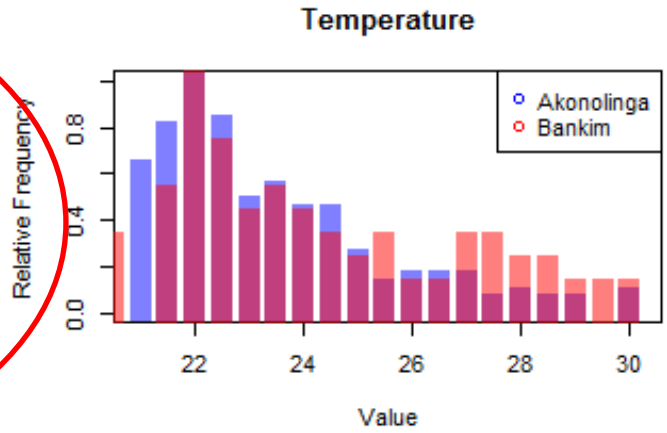


2 Why the two regions are so different?







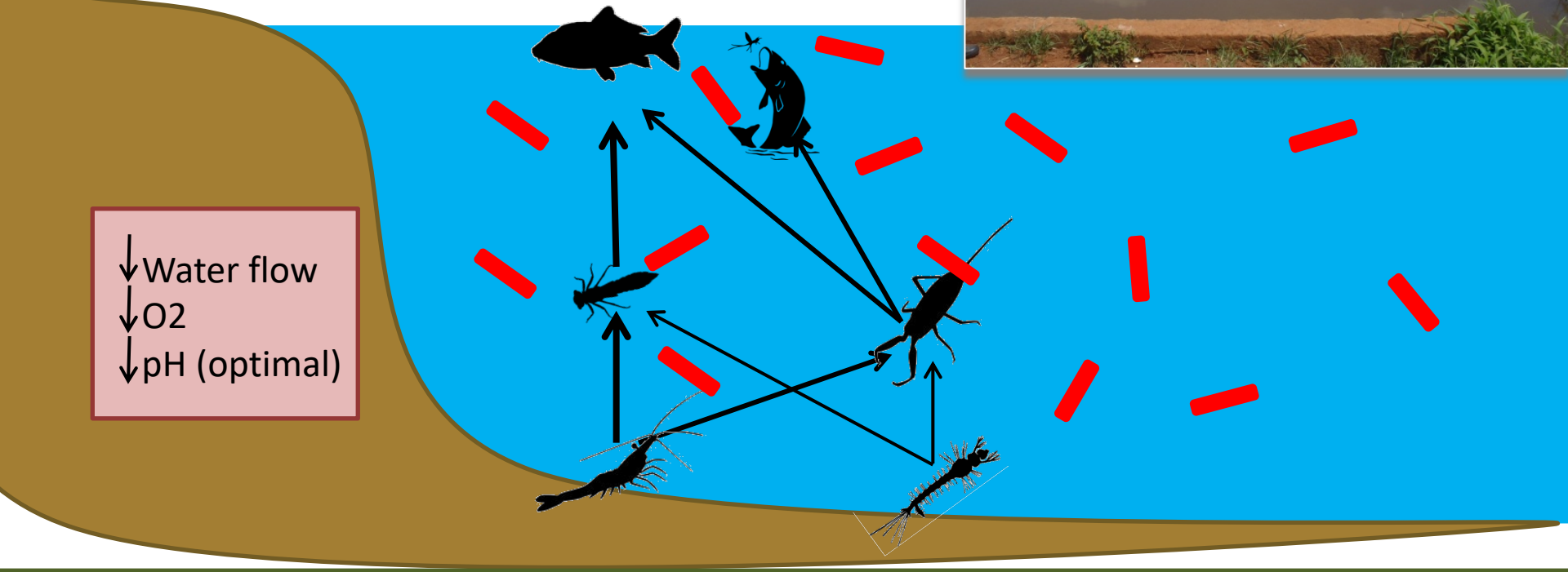


Optimal *pH* for *MU* [5.8-6.5]

2 Our theory

Scenario 1: Favourable physico-chemical conditions

Free living stages
&
Environmental transmission to aquatic organisms

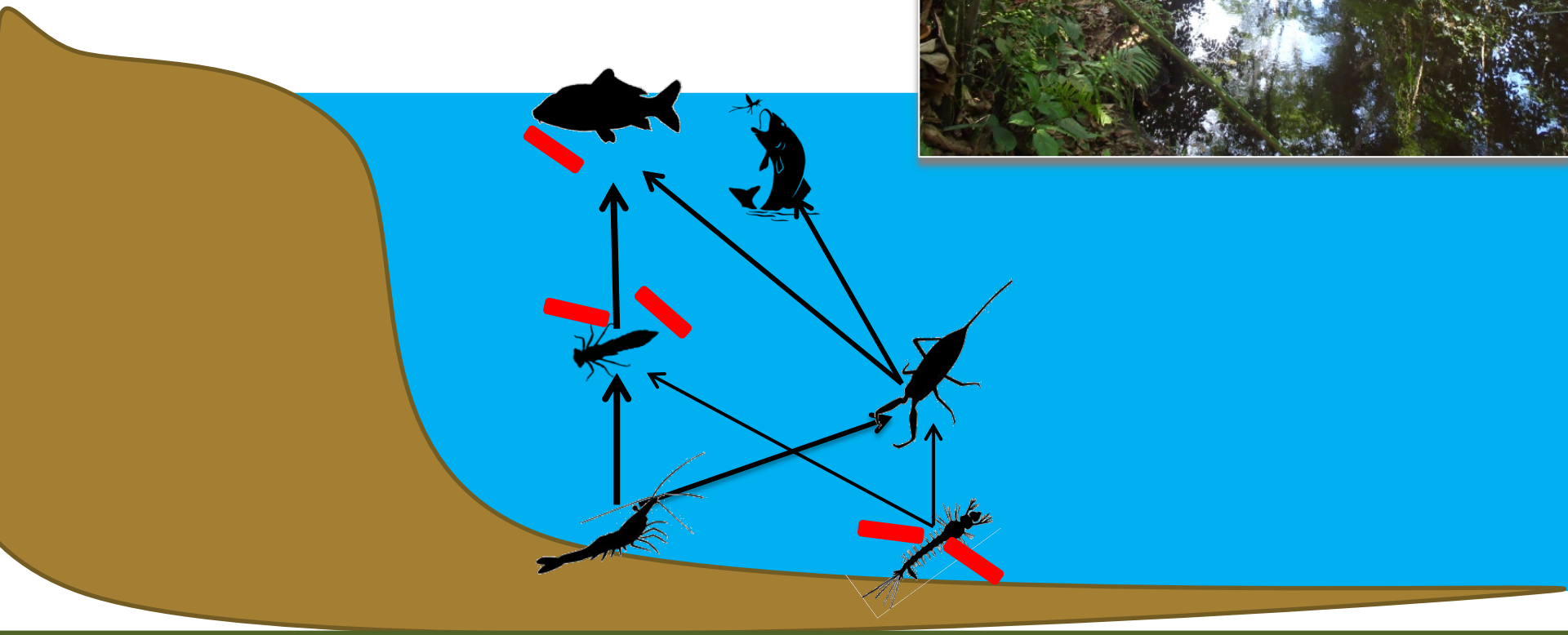


↓Water flow
↓O2
↓pH (optimal)

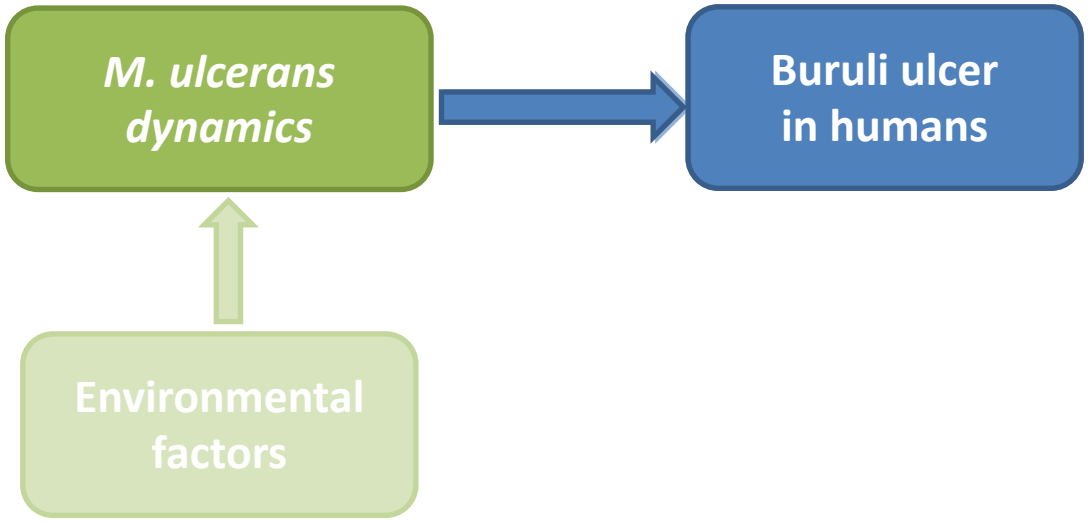
2 Our theory

Scenario 2: Adverse physico-chemical conditions

Mostly intra-host
&
Trophic transmission

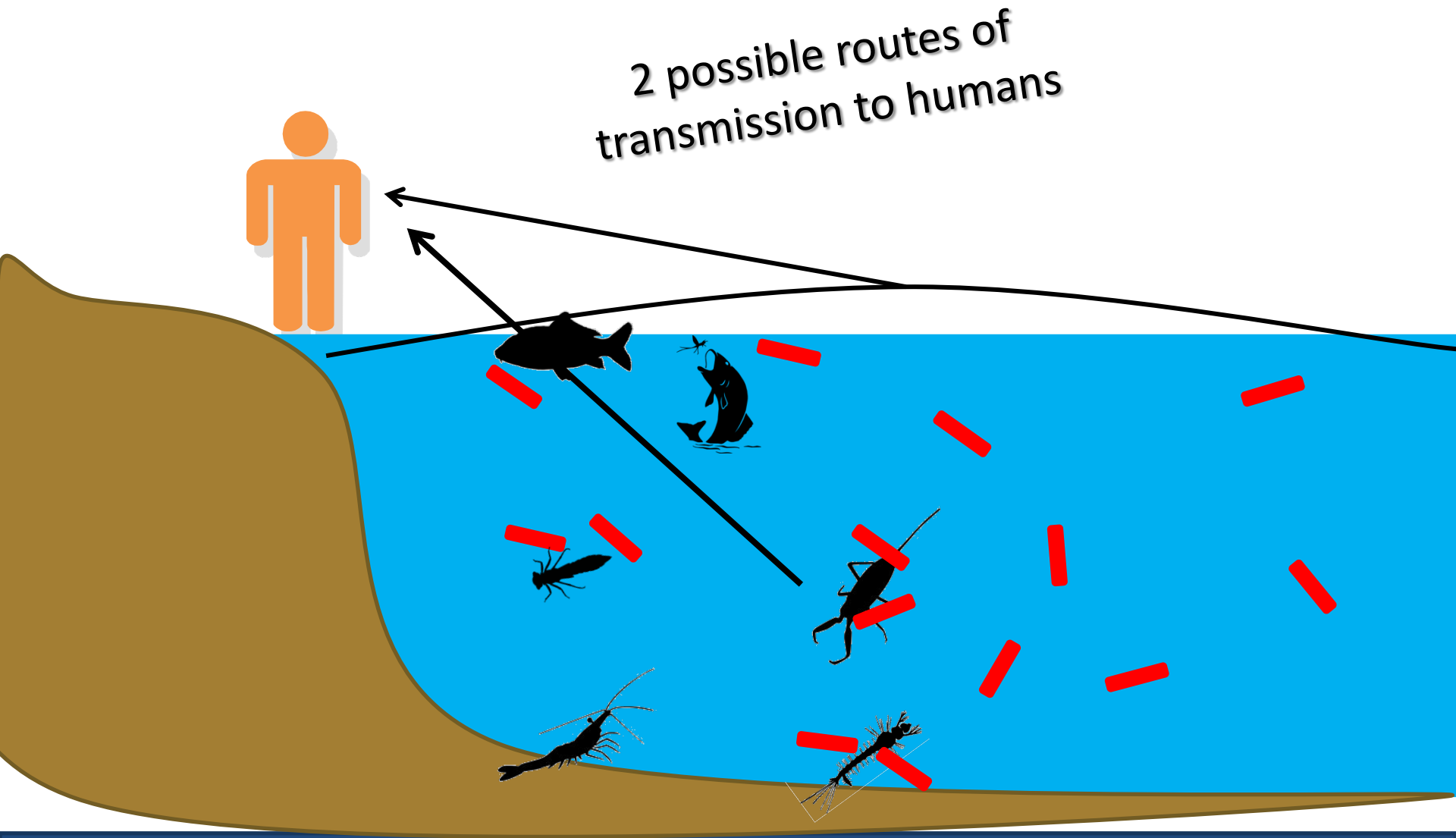


What type of modeling is necessary to answer my question?



MATHEMATICAL MODELING TO UNDERSTAND BU TRANSMISSION

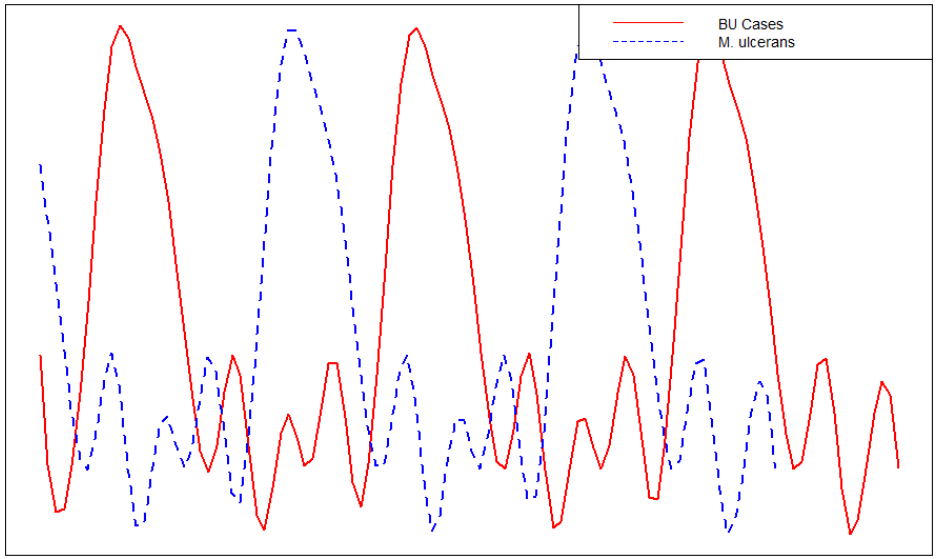
Introduction

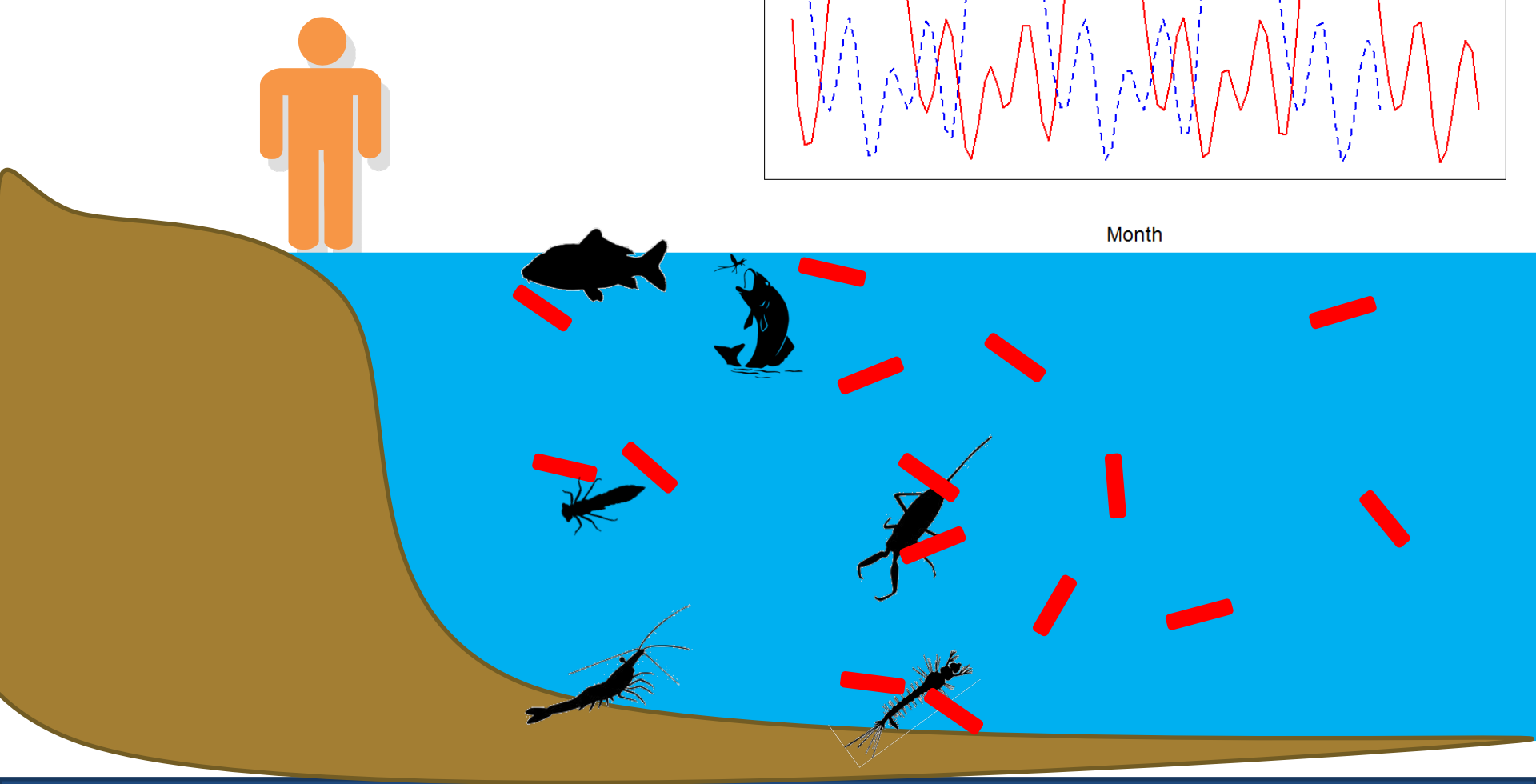


Transmission of MU to humans

Introduction

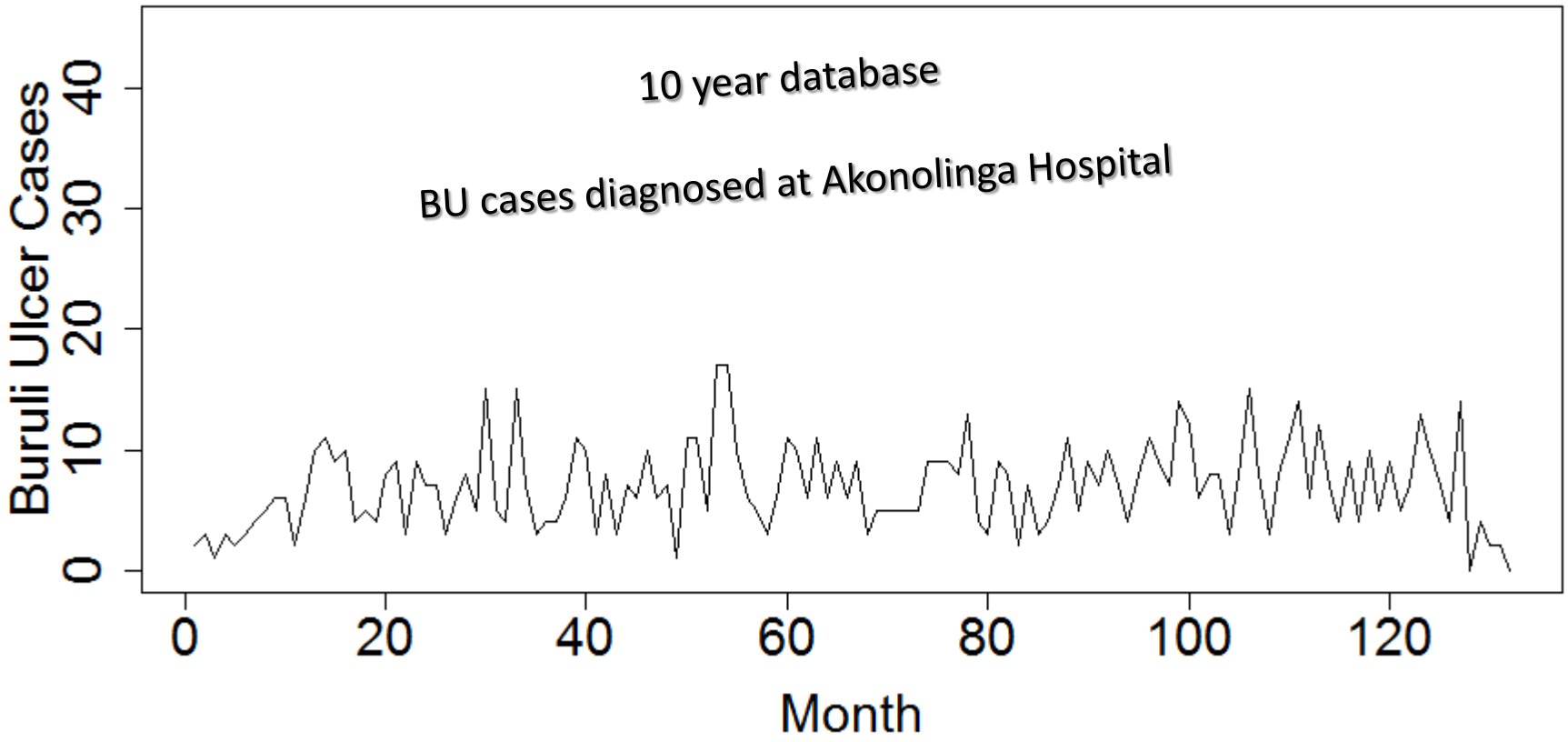
Dynamic model



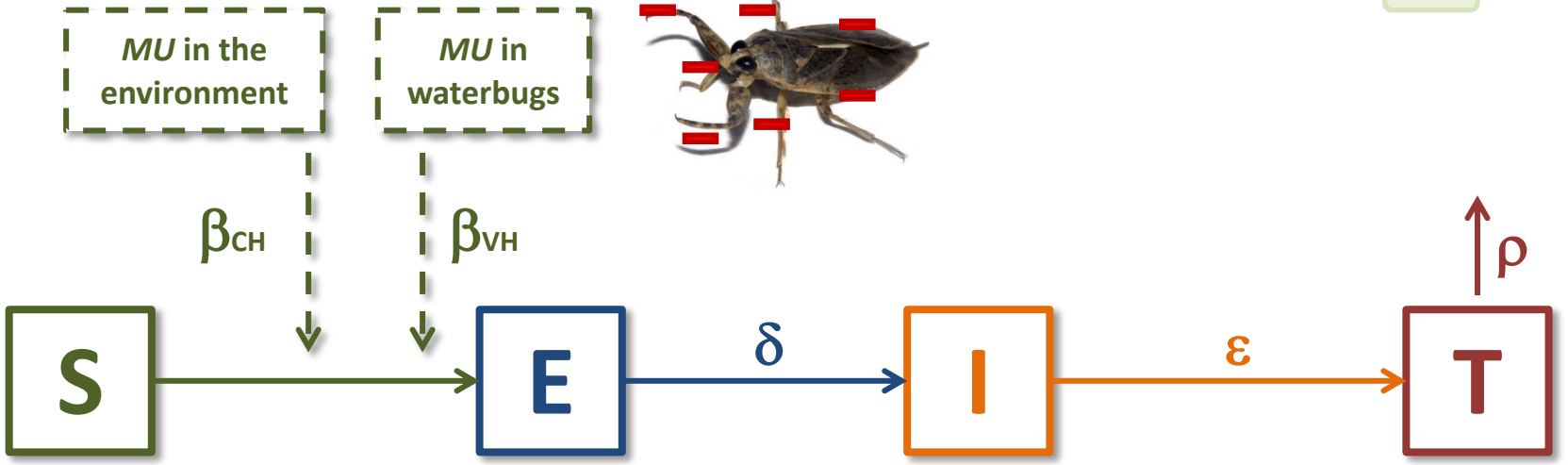


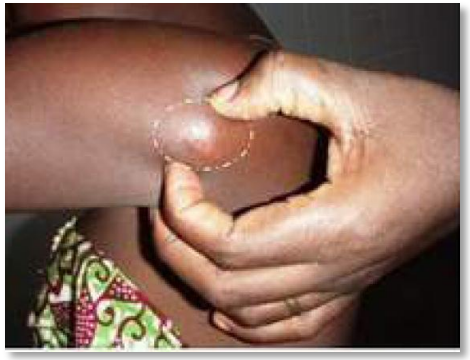
Transmission of MU to humans

3 Temporal data



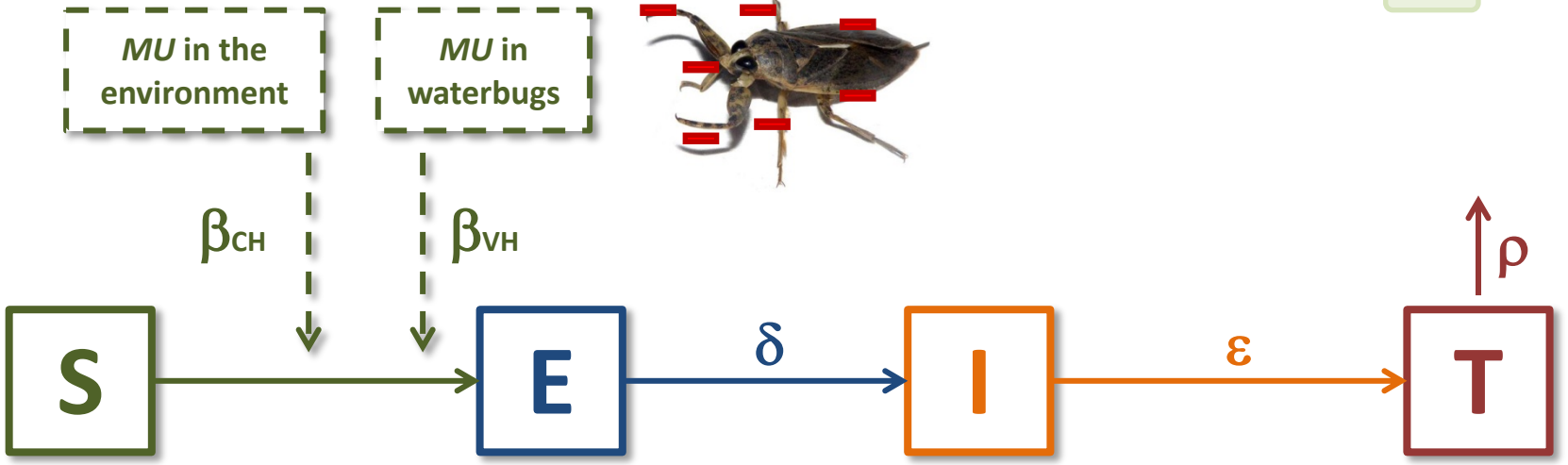
3 Mathematical model framework





Transmission of MU to humans

3 Mathematical model framework



Mathematical Model

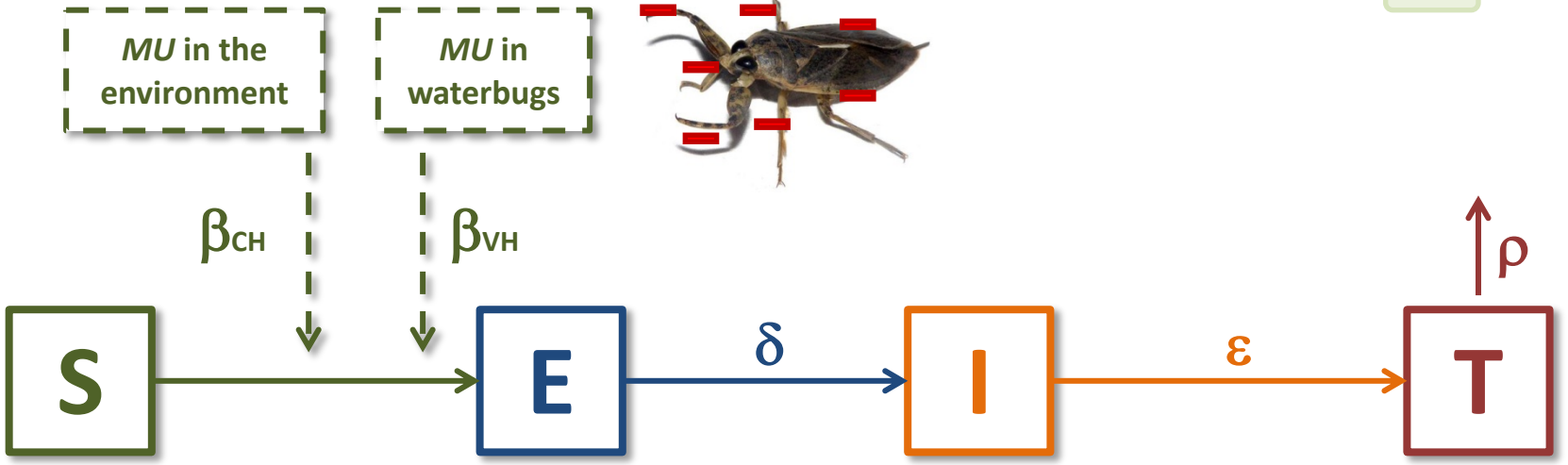
$$\frac{dS}{dt} = \mu N - \lambda_{CH}(Month_i)\, S - \lambda_{VH}(Month_i)\, S - \mu\, S$$

$$\frac{dE}{dt} = \lambda_{CH}(Month_i)\, S + \lambda_{CH}(Month_i)\, S - \sigma\, E - \mu\, E$$

$$\frac{dI}{dt} = \sigma\, E - \varepsilon\, I - \mu\, I$$

$$\frac{dT}{dt} = \varepsilon\, I - \gamma\, T - \mu\, T$$

3 Mathematical model framework



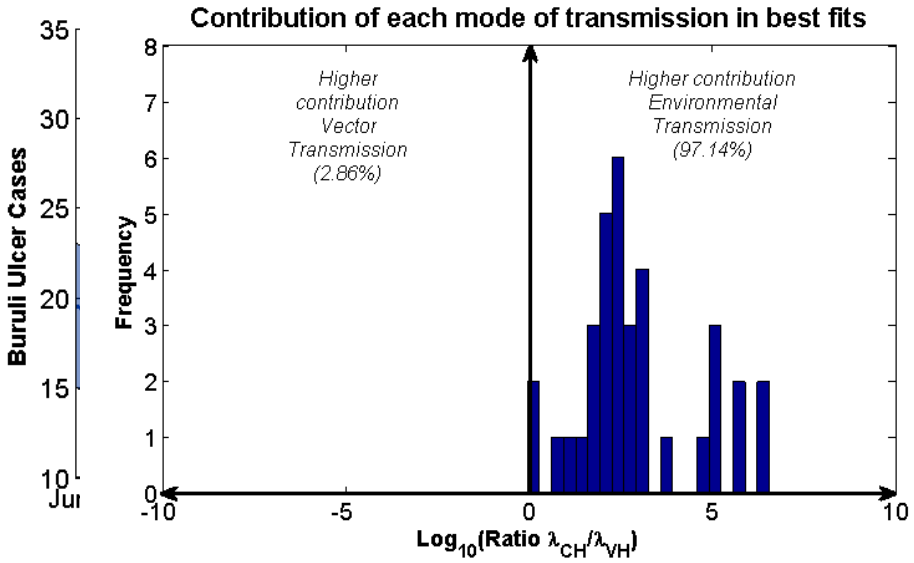
Model simulations to account for:

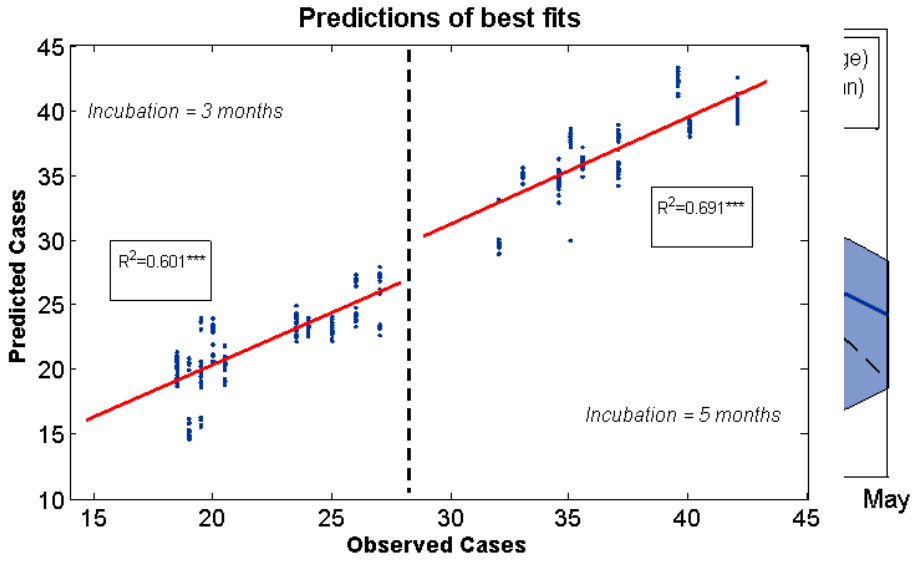
- A range of initial parameters
- Uncertainties in rates of incubation (δ) and seeking treatment (ε)
- Different proxies of waterbug tranmsission and environmental transmission
- Linear risks or thresholds in the relationship MU-BU

Comparison of model fit using AIC and selection of best performing (2 AIC)

Results for Buruli ulcer temporal dynamics

Best temporal fit





Environmental transmission >>>> water bug transmission

MU environmental concentration as linear predictor of BU cases

AT THIS STAGE WE ARE ALMOST DONE…

Manuscript writing and submission

- What are the main results that provide the answer to my question?
  - 1 to 3 graphs
  - 1 to 3 tables
- What is the journal that best fits my study?
  - Scope, audience, impact factor, math focus
- How do I present my manuscript?
  - Introduction: set the stage to your question
  - Methodology: describe explicitly all steps for replicability
  - Results: clear and concise
  - Discussion: explain how your study improves previous knowledge

MODELING IN PRACTIVE: THE LIFE CYCLE OF A MODELING PROJECT, FROM CONCEPTION TO PUBLICATION

- The example of Buruli ulcer in Cameroon -

Andrés Garchitorena

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Associate Scientific Director, PIVOT Madagascar

E²M² Workshop
Ranomafana, January 2020